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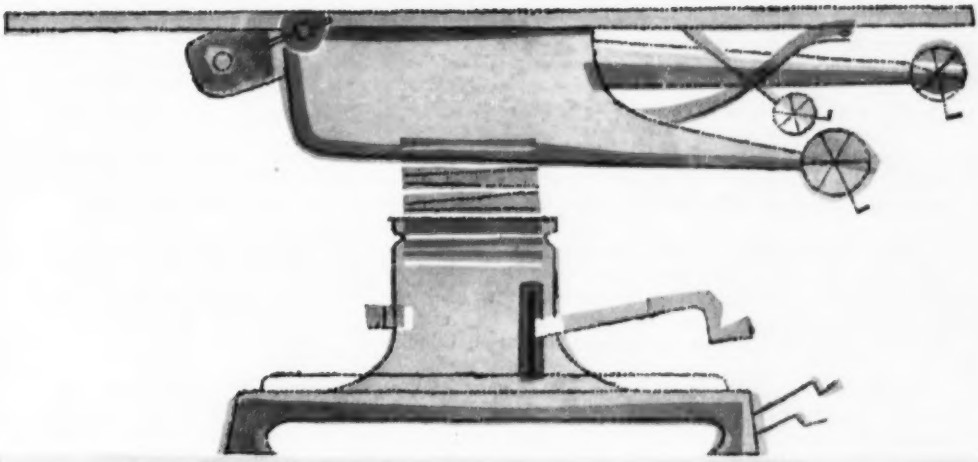

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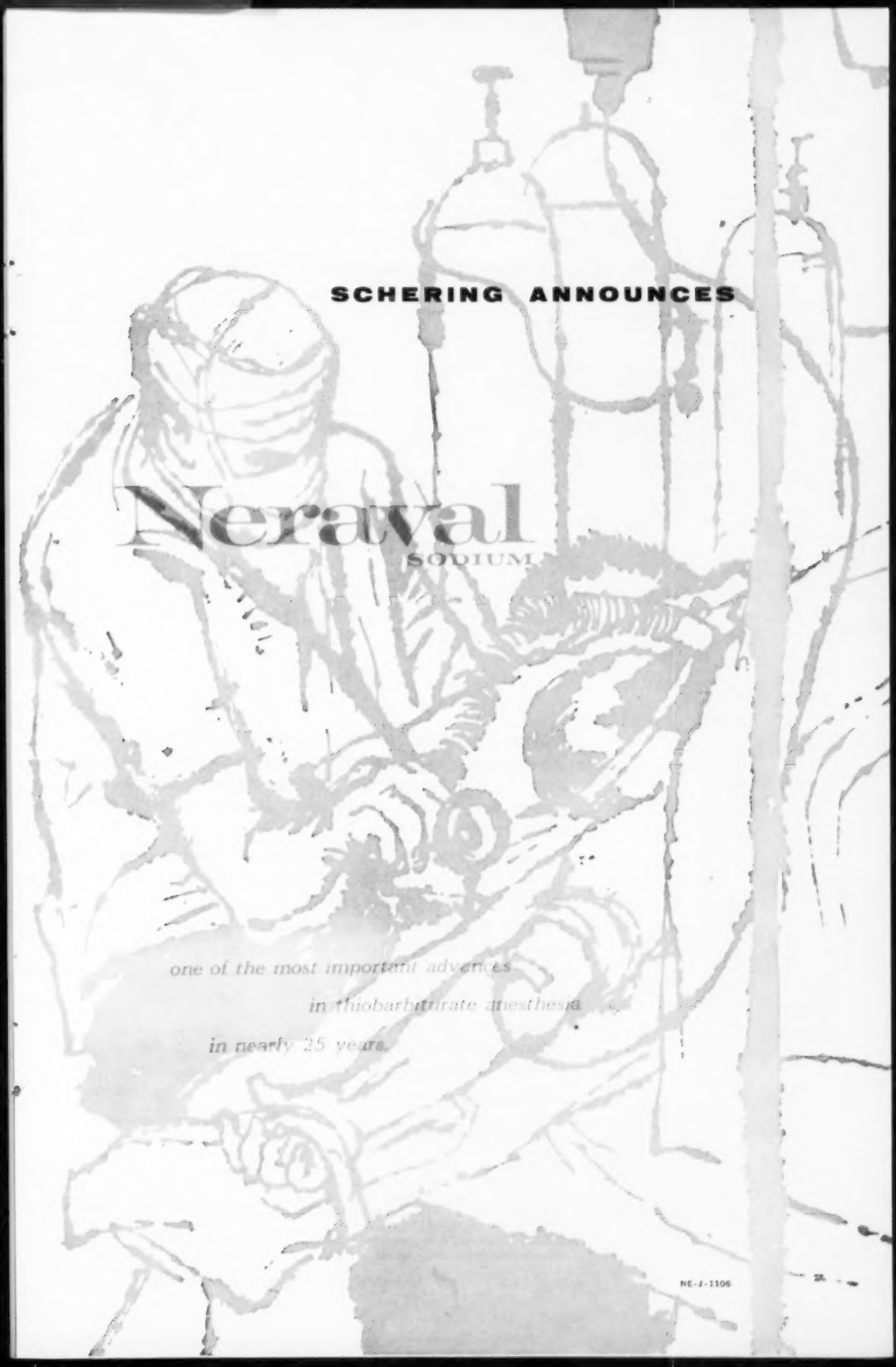
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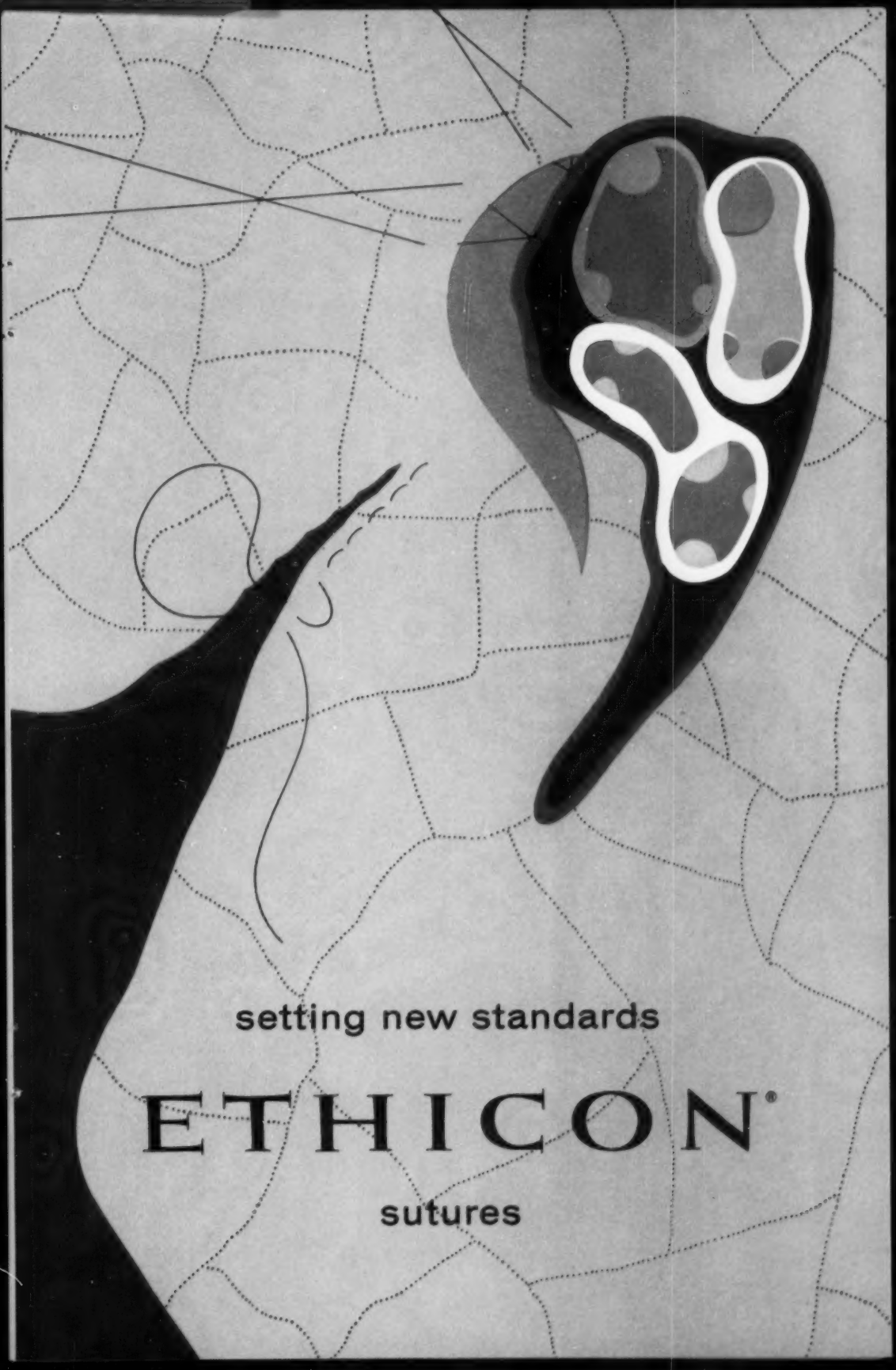
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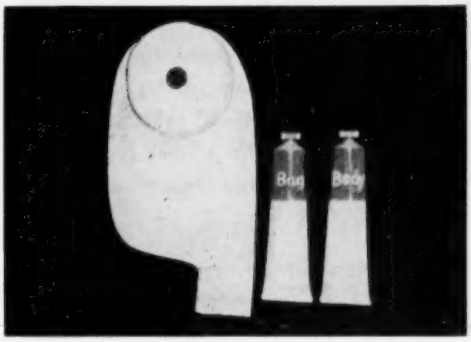

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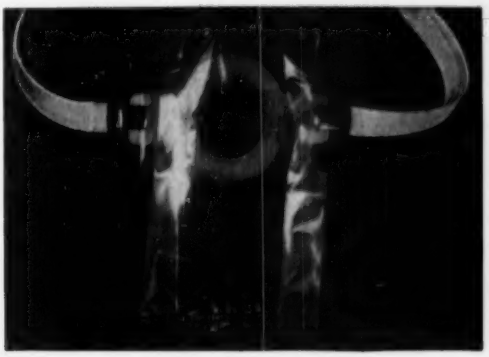

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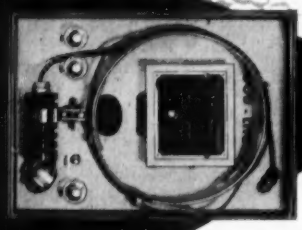

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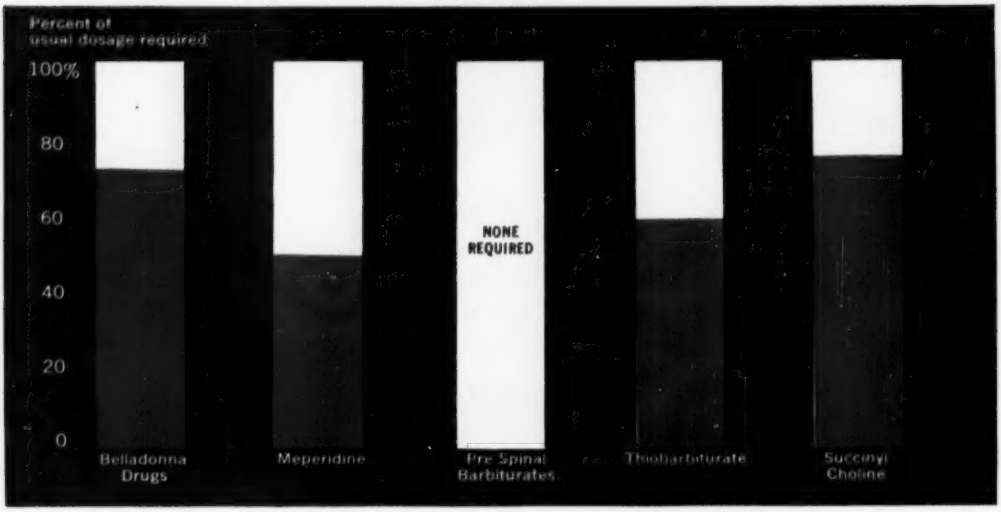

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Eleven Years' Study at the University of Minnesota

CLAUDE R. HITCHCOCK, M.D., Ph.D., and SAMUEL HOROWITZ, M.D., Minneapolis

Death still claims a high percentage of seriously burned patients. Where 55% or more of the body surface is severely burned, the mortality rates are in the range of 85% in most clinics. Owing to a better understanding of fluid and electrolyte balances in patients with severe burns, these critically injured people often survive the initial "shock" period of the postburn state only to succumb with sepsis, hepatic failure, cardiac complications, or other types of medical emergencies in the later postburn period.

We are immediately aware that further advances must be made in effecting earlier, more complete grafting of larger burned areas, with an over-all reduction of the "chronic," or reconstructive, phase of the problem. In a recent report four American medical centers failed to show any improvement in mortality of burned patients in the 15%-35% body-surface burn group, and also in the 70%-100% body-surface burn group, when they compared experience during the year 1944 with the year 1951.

Amspacher and Cloud have separated deaths following severe burning into three etiologic categories: Death on the day of injury is usually from a respiratory disturbance; death during the period from the 2d to the 10th or the 12th day after burn is usually attributable to serious fluid and electrolyte disturbances, and death after the 13th to the 14th day after burn usually relates to infection.[5] In 1950 R. K. Brown and Dziob reported that in their experience death after the second to the third postburn day was usually from liver necrosis or severe infection.[9]

The development of methods permitting homografts to survive indefinitely as permanent surface covering for the recipient body would undoubtedly improve the chances for survival of severely burned patients. Recent work at the University of Minnesota by Good and Varco lends support to our hopes for possible "de-individualization" of a recipient such that he can accept, and retain permanently, homografted skin from any available donors. Even though we cannot as yet "de-gammaglobulinize" a person, and in spite of the present contraindications for inducing this pathologic state in seriously burned patients, the long-term survival of homografted skin on a patient afflicted with idiopathic agammaglobulinemia is a signal event.[21]

Burned Patients at University of Minnesota Hospitals, 1945 through 1955

During the 11 years from 1945 to 1955 a total of 170 patients were treated at the University of Minnesota Hospitals for

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TABLE 1.—*Mortality for All Burned Cases at University of Minnesota Hospitals from January, 1945, to January, 1955*

	Patients	Deaths	Mortality, per Cent
1st-and 2d-degree burns only	31	3	9.7
3d-degree burns	139	17	12.2
Totals	170	20	11.7

Deaths in the Group* with First-and Second-Degree Burns

Age	Body Surface Burned, per Cent
1 yr	8
4 mo	20
4 days	5

* Seventeen patients in this group were under 6 years of age.

burns or problems associated with burns. Only 45 (25%) were admitted initially to the University Hospitals (within three hours of burning) and received emergency as well as late care there. For patients admitted within the early postburn period, the average time interval from trauma to admission was 29 days. A small group of patients (19) was admitted an average of eight months after burn trauma for surgical correction of contractures and other sequelae.

Yearly admissions varied from 10 to 28 patients per year, and there were 139 patients with third-degree burns and 31 patients with burns of only first and second degrees. A total of 385 primary skin-grafting procedures were performed on this group, and an additional 64 operations were performed for complications and sequelae of the trauma.

TABLE 2.—*Mortality for Third-Degree Burns of 15% or More Body Surface*

Body Surface Burned, per Cent	Patients, No.	Deaths
15	17	1
20	15	3
25	15	4
30	5	1
35	5	0
40	6	1
50	3	1
55	2	0
65	2	2
70	1	0
75	1	1
80	1	1
	73	15 (20.5% mortality)
50% or more of body surface burned	10	5 (50% mortality)

A comparison of mortalities for various depths of burning is presented in Table 1; three deaths occurred in the 31 patients with first- and second-degree burns (9.7% mortality), and all deaths were in infants under one year of age. Seventeen of the thirty-one patients with first- and second-degree burns were under 6 years of age. There were 17 deaths among the patients with third-degree burns, or a mortality in this group of 12.2%. The over-all mortality for the 170 patients was 11.7% (20 deaths).

In Table 2 patients are divided according to the area of the skin burned full thickness, or third degree. Only patients with 15% or more of the body surface involved are represented. The mortality for this group of 73 more seriously burned patients is 20.5% (15 deaths). In 1953 Moyer published a mortality of 23.8% for a group of 315 patients with burns involving 15% or more of the body surface; while direct comparisons are invalid, since we cannot accurately compare these series as to earliness or lateness of admission to the hospital providing definitive care, the similarity of these two percentages is striking. Special note should be made in Table 2 of the five patients in our series surviving 40% burns, the two survivors of 50% burns, the two survivors of 55% burns, and the one survivor of a 70% burn.

Table 3 represents all cases of third-degree burns covering 15% or more of the body surface arranged in four age groups.

TABLE 3.—*Mortality for Various Age Groups of Patients with Third-Degree Burns of 15% or More of Body Surface*

Age group, yr.	Patients, No.	Deaths	Mortality, per Cent
0-6	22	5	22.7
7-15	13	2	15.3
16-35	17	3	17.6
36 and over	21	5	23.8
	73	15	20.5

Analysis of the 15 deaths in the patients with third-degree burns covering 15% or more of their body surface reveals a somewhat higher mortality in the extremes of life, the infants and the aged. From Table 1 and 2 we see that less extensive burns, in the range of 9%-10%-15%, caused death in the patients 50 years of age and over. Small infants lost their lives from burns of only first- and second-degree severity, as noted in Table 1.

An analysis of the 17 deaths occurring in the total group of patients with third-degree burns, including those burned to an extent less than 15% of the body surface, is presented in Table 4. Two deaths were attributed to "shock," and both patients were in the infant group. One, a one-and-one-half-year-old child with a 30% burn, died on the eighth day after burning with persistent low blood pressure and anuria; the other, a 3-year-old child suffering from an 80% body burn, died in shock during the first 24 hours after the burning.

Infection was a major cause of death in 4 of the 17 patients and a contributing factor in 1 additional patient. All these patients had positive blood cultures indicating septicemia. Death occurred from the 15th to the 59th day after burn in the four patients and on the 6th day after burn in the case listed with sepsis as the probable etiology. Two patients, aged 2 and 16 years, died after cardiac arrest incidental to surgery on the 80th and the 148th day after burning. The importance of the heightened sensitivity of the myocardium, due to the mild but chronic acidosis common to burned patients, must be fully appreciated at the time of anesthesia or surgery.

Another child, an 8-year-old girl with a 65% third-degree burn involving a major portion of her trunk and head, died after an occult perforation of the stomach by a firm plastic intragastric feeding tube. She had been successfully grafted on five occasions with homografts and autografts, and only 15% of the burned area remained

TABLE 4.—*Analysis of Deaths Following Third-Degree Burns*

Age Group	Age, yr.	Body Surface Burned, per Cent	Cause of Death	Days Lived
0-6 yr.	1½	30	Shock—anuria	8
	2	18	Aspiration asphyxia	13
	2	25	Cardiac arrest—recovery room	80
	3	50	Sepsis—probable	59
	3	80	Shock (died within 24 hr.)	0
7-15 yr.	8	65	Perforation of stomach (tube)	252
	9	65	Sepsis—hepatic failure	35
16-35 yr.	16	25	Cardiac arrest (after surgery)	148
	22	40	Air embolus	22
	24	75	Dehydration—fever—sepsis	6
36 yr. and over	36	20	Sepsis (narcotic addict)	31
	53	25	Sepsis (Pseudomonas)	15
	57	9	Homologous serum jaundice	67
	74	18	Pneumonia (aspiration)	31
	75	15	Heart failure (fibrillation)	28
	76	10	Cerebrovascular hemorrhage	38
	80	25	Heart failure	39

to be covered at the time of death, on the 252d day after burning. Firm gavage tubes of this type can be dangerous, particularly if allowed to remain in the stomach for several days, as in this instance. We now recommend soft rubber tubes or thin polyethylene tubes for gavage feedings, with the tubes withdrawn each evening.

At autopsy this child's liver was greatly enlarged, soft, and yellow, and sections confirmed a diagnosis of severe yellow atrophy. Hepatic damage is a serious and frequent complication of the prolonged recovery period of the severely burned patient. Several factors contribute importantly to this phase of the rehabilitation problem in the burned patient. The liver may be damaged from prolonged toxicity due to sepsis and tissue breakdown; there are deleterious effects from the constant drain on the protein stores of the body over a protracted period of time; there is possible hepatic injury due to continual therapy with a wide spectrum of antibiotics, and possible liver damage from repeated blood and plasma transfusions. It is conjectural whether the liver of this child could have recovered had the untoward gastric perforation not occurred. However, such experiences emphasize the importance of providing either permanent or temporary coverage for all burned areas as early and quickly as possible. A reduction in the time involved in covering these seriously burned patients with permanent skin will undoubtedly lessen the risks of such deleterious effects on the liver and other parenchymal organs.

Fifty-four of the burned patients arriving at the University Hospitals after initial therapy in their home community were admitted within 15 days after burning. The remainder came in as late as 50 to 60 days after being burned, having been cared for in local hospitals during this time. Such delays in transporting patients with severe burns to the point of definitive care are unwarranted. If a program of skin grafting cannot be carried out in the local hospital, these patients deserve immediate transfer, as soon as practicable, to a unit equipped for the job. Ambulance transport can be safely and comfortably accomplished by using petrolatum (Vaseline) gauze and bulky dressings over the burned areas en route. These can be removed as soon as the patient arrives at the point of final therapy.

The apathy inherent in the management of a "chronic surgical problem" of this kind must be vigorously combated by everyone caring for these patients. Repeated delays in transport, delays in scheduling for surgery, delays in transfusing with whole blood at the earliest tendency toward anemia, delays in forcing a high caloric intake, all contribute to unnecessary waste of valuable weeks, unduly prolonging the serious effects of the pathologic state of the postburn period. All physicians and nurses involved in the care of burned patients can contribute significantly to the patient's welfare in this regard; constant vigilance against procrastination and unwarranted delays of the various types is mandatory.

Replacement Therapy in the Immediate Postburn Period

Current ideas of replacement therapy for burned patients are an outgrowth of the 1942 meeting of the Committee on Burns of the National Research Council. Under the chairmanship of Dr. I. S. Ravdin, recommendations were made for replacement therapy predicating fluid requirements on the area of skin surface burned. The final plan adopted by this group provided 75 cc. of plasma and 75 cc. of saline to be administered for each 1/100 (1%) of body surface burned, the total amount to be given during the first 24 hours after burn. This initial replacement formula ignored the relationship of tissue mass to the problem of translocation of body fluids.[13]

The wisdom of providing electrolyte replacement as well as protein replacement was proved subsequently by Cope and Moore. Their studies revealed that the concentration of protein in burn bleb fluid

is equal to one-half to two-thirds that of normal plasma, whereas the electrolyte pattern and concentration of burn bleb fluid are equal to those found in normal plasma. These classic studies assessed the pathologic physiology of body fluids in the burned patient by means of radioactively tagged protein and red cells. The authors were soon impressed with the inordinate quantities of saline and water given as initial replacement therapy to the burned patient when replacement needs were calculated on the rising hematocrit and hemoglobin values. One early-study patient in their series received during the first 24 hours after burn a total of 21,313 cc. of fluid, and the urine output was 6855 cc. for this 24-hour period (1947). It was apparent that "mass of tissue" constituting the body of the organism needed to be considered in replacement needs.[13]

The significant studies of Evans, Purnell, and associates were reported in 1952. They found that dogs, burned experimentally, lost plasma in the amount of 1 cc. for each 1/100 (1%) of body surface burned for each kilogram of weight; this rather constant loss was manifest usually by the sixth hour after burn.[17] Their clinical studies, reported in 1952, revealed deaths from pulmonary edema secondary to overinfusion of colloid materials and electrolytes within the first 24 hours after the burning. A patient weighing 61 kg. and injured with a 92% burn received 14,460 cc. of fluid within the first 24 hours, and all of this was given as colloid- or electrolyte-containing solutions (5300 cc. of plasma and 9160 cc. of saline). Pulmonary edema was severe in this case, and the patient subsequently died. Another patient, 19 years old and weighing 57 kg., was injured by a 63% burn; he received 16,000 cc. of fluid within the first 24 hours and died in 4 days of severe pulmonary edema.

Several important guiding principles were established by these authors, and they bear repetition here because of their impact upon prevailing ideas in this field today.

1. Whole blood and plasma should be used in equal amounts for colloid replacement.

2. Colloid materials in the amount of 1 cc. per 1% of body surface burned per each kilogram of weight should be given in the first 24 hours.

3. Saline solution in equivalent amounts (1 cc. per 1% burned per kilogram) was to be used.

4. The hourly urinary output was recognized as an effective measure of adequacy of fluid replacement.

5. The necessity for rapid administration of proper fluids immediately after the burning incident was recognized.

6. Evans, Purnell, and associates emphasized need for caution in the infusion of calculated amounts of fluids to patients over 50 years of age and also to patients burned in excess of 50% of the body surface.

The practicality of this program of replacement therapy, based upon sound experiment, caused it to be widely applied during the past few years.

Recently the experience of Amspacher and the Surgical Research Unit at Brooke Army Hospital has been popularized throughout the country. Their immediate management of severely burned patients calls for replacement therapy with colloid materials in the amount of 0.5 cc. per 1/100 (1%) of body surface burned per kilogram of weight, electrolyte-containing solutions in amounts of 1.5 cc. per 1/100 (1%) of body surface burned per kilogram of weight, and 1000 to 1500 cc. of dextrose in water to cover insensible loss. This total amount of fluid is recommended for the first 24-hour period, and roughly one-half of this amount during the second 24-hour period.[3-5,36]

Recent experience at the hospitals of the University of Minnesota and the Minneapolis General Hospital has substantiated the adequacy and effectiveness of the planned replacement program of Evans and Purnell. When small children and patients over 55-60 years of age have received electrolyte-solution replacement according to the regimen of the Brooke General Army Unit (1.5 cc. per 1% burned per kilogram), pulmonary edema has been a disturbing complication. However, the importance of using some quantity of NaCl in the initial replacement therapy has been classically demonstrated

recently at the Minneapolis General Hospital.

For several years, during a study of fluid and electrolyte changes in patients with burns covering more than 30% of their body surface, patients have received only plasma and dextrose solution during the first 24 hours after the burn. Serum concentrations of sodium, chloride, potassium, carbon dioxide, and proteins were evaluated against urinary excretions of these materials. Quantities of fluid and colloid to be replaced were determined by a formula of 1 cc. plasma per 1% of surface burned per kilogram weight during the first 24 hours and an equal amount of dextrose in water in the same period of time. Sodium and chloride replacement during the second and the third postburn day was determined by serum concentrations prevailing 24 hours after the burning.

A young woman of 18 was admitted with an 80% third-degree burn, arriving in the hospital 45 minutes after her accident. Table 5 details the replacement therapy she received during the first 48 hours. According to the formula of the study program, she received 4325 cc. of plasma and 4000 cc. of dextrose (5%) in water. Urinary output for the 24-hour period was 1650 cc.

Twenty-four hours after arrival in the hospital the patient was completely irrational and difficult to manage; the serum sodium at this time was 110 mEq. per liter, and the serum chloride was 75 mEq. per liter. The patient was in a severe state of "water intoxication." Such a condition of water logging of somatic cells in all parts of the body, due to the severe degree of hyponatremia and hypotonicity of circulating plasma and interstitial fluid, is one of the most serious electrolyte disturbances encountered by the human body. Darrow and Yannet first focused attention on this phenomenon, and many investigators have subsequently confirmed it.[41] Water moves into the cells in the face of lowered sodium levels of the extracellular fluid, and it makes

TABLE 5.—*Water Intoxication from Initial Imbalance in Replacement Therapy*
Patient with 80% Body Burn at Minneapolis General Hospital

Patient:	Admitted: July 15, 1955	
Wt., 57 kg.	45 min after 80% burn from explosion in home	
Age, + 18 yr.		
Calculated intake for first 24 hr.	(Evans Formula)	
Colloid	57×50×1=	2,850 cc.
Electrolyte	57×50×1=	2,850 cc.
Insensible loss		2,000 cc.
		7,700 cc.
Replacement therapy received for first 24 hr., calculated according to study program		
Plasma (colloid)		4,325 cc.
Dextrose 5% in water		4,000 cc.
		8,325 cc.
Urine output in first 24 hr.		1,650 cc.
Chemistries 24 hr. after burning		
Sodium		110 mEq./liter
Chloride		75 mEq./liter
Potassium		3 mEq./liter
Patient was irrational with severe water intoxication at this point (note sodium of 110)		
Replacement therapy for second 24 hr.		
Plasma		500 cc.
Dextrose in water		4,800 cc.
Late in day sodium chloride was given as hypertonic solution, 388 mEq. or 22.5 gm. of NaCl		
		5,300 cc.
Urine output in second 24 hr.		2,950 cc.
Chemistries 48 hr. after burning		
Sodium		135 mEq./liter
Chloride		94 mEq./liter
Carbon dioxide		27 mEq./liter
Patient recovered from water intoxication (cerebral edema) by 60 hr. after burn		

no difference whether dilution of the extracellular space occurs from addition of inordinate quantities of water or subtraction of sodium; the end-result is the same. The balance of intracellular water with extracellular water is governed by the concentration of extracellular sodium at any given moment. Severe central nervous system disturbances are always present in this condition, and convulsions and seizures frequently occur. Unless the severe sodium deficit is corrected immediately with hypertonic salt solution, death follows quickly. Late in the second day of admission, this patient received 388 mEq. of sodium (22.5 gm. of sodium chloride) as a hypertonic solution, and the serum sodium 48 hours after burning was then 135 mEq. per liter. Twelve hours later, by the sixtieth postburn hour, this patient was more rational and her sensorium was clearing.

It is obvious that an attempt to prevent pulmonary edema by withholding sodium in these circumstances is fraught with great hazards. With serious loss of colloid and fluid from the body through burned skin and into large blebs, and with extensive translocation of fluids from the circulatory compartment into the interstitial compartment, large quantities of fluid must immediately be replaced to the burned patient. Under these pathologic conditions strict maintenance of accepted normal valves for certain electrolytes may be injurious to the patient. Conversely, however, obviously severe distortions of the electrolyte pattern must be prevented, as exemplified above. Carl Moyer has aptly stated this problem and concept in a recent monograph: "Another aspect of body fluids about which little is known, and which pertains especially to therapeutics is the peculiarities of the volume, the concentration and the composition that are most conducive to recovery from illness. At present it is assumed that, in those who are ill, the restoration or maintenance of the values which obtain during health is most conducive to recovery. This assumption is apt to be untrue in many instances. In other words, it is possible that during illness certain deviations from normal of the milieu intérieur may be more conducive to the restoration of a feeling of well being than the maintenance of, or restitution to, normality."[30]

We believe that this concept applies significantly to patients with serious third-degree burns. Our aim regarding initial replacement therapy probably should be to (1) compensate for the large abnormal losses and translocation of circulating fluid, electrolyte, and protein; (2) prevent hyponatremia and undue concentration of the red cell mass, and (3) maintain the patient at a slightly reduced level of serum sodium tending to prevent pulmonary edema. Since many burned patients suffer a greater or less degree of tracheal bronchial irritation from hot gasses and therefore are predisposed to pulmonary edema, the latter consideration seems important to us for optimum management of these serious cases. In our experience the Evans formula, as originally published, has guided our early replacement therapy most adequately and safely. If we change it at all, we shade the electrolyte replacement downward slightly. Therefore, our basic replacement therapy for adults is as follows: colloid—1 cc. per 1% burned per kilogram weight (one-third to one-half of this amount as whole blood); electrolyte—0.75 to 1.0 cc. per 1% burned per kilogram weight, and dextrose in water—1000 to 2000 cc. Figure 1 demonstrates the rate of replacement for the first 24 hours after burn.

Period of Diuresis

Data from the Minneapolis General Hospital reveal that the diuresis resulting from the mobilization of the extensive interstitial edema fluid into the circulating blood usually begins by the 30th or the 40th hour after the burn trauma. This mechanism of bodily adjustment must be fully appreciated, and a marked reduction in administered fluids instituted on the second and subsequent days

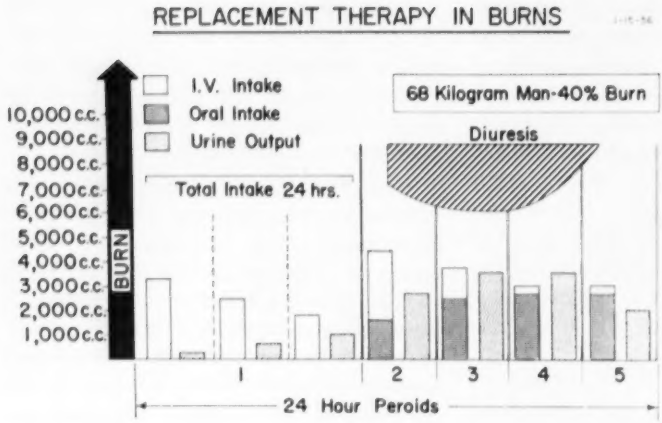

Fig. 1.—Relationship of fluid intake to early period of diuresis in a patient at Minneapolis General Hospital. Diuresis usually begins between the 30th and the 40th hour after burn. Note the reduction in fluid administered on the second and subsequent days after burn.

after burn, or hypervolemia and pulmonary edema can result. In Figure 1 is portrayed the relationship among administered fluid, urinary output, and diuresis in a patient at General Hospital. Note that urinary output continually increased in this man up to the third and the fourth day after burn, while the fluid intake was progressively decreased. By the fifth day after burn this patient was well stabilized on oral intake of food and fluids, with an occasional unit of whole blood administered intravenously.

The most satisfactory gauge for the adequacy of fluid replacement during the first few days after burn is an hourly recording of urinary output. This method has been eminently successful in our hands, and other authors report similar successes. There is a general consensus among authors that fluid replacement cannot safely be determined by elevations in serum hemoglobin and hematocrit values. With an adequate urinary flow, the hemoglobin usually does not rise above a level of 18-19 gm. per 100 cc., even during the period of severest translocation of circulating fluid.

Therapy with Whole Blood

Good experimental evidence supports the apparent clinical benefits of whole blood transfusions in the therapy of severely burned patients. In 1952 Quinby and Cope published studies of red cell destruction during burn trauma, assessed through the use of tagged red blood cells made radioactive with radioactive iron and chromate. They reported destruction of 7%-10% of the red cell mass in a patient suffering from a 35% full-thickness burn.[35] However, it must be recognized that the loss of red cell mass is small compared with the more massive losses of plasma.

In the absence of blood transfusions early in the postburn period, an anemia of greater or less severity results. Use of whole blood to account for one-third to one-half of the initial colloid requirement provides early compensation for loss of red cell mass as well as combating shock. We have never seen untoward hemoconcentration as a result of this therapy.

In the later stages of therapy, during reconstructive surgery, whole blood is absolutely vital if hemoglobin is to be maintained near optimum levels. The importance of an adequate red cell mass to the healing of extensive wounds is well known. In adult patients free of cardiac complications, the hemoglobin should approach 15 gm. per 100 cc. assessed during an adequate state of hydration.

Treatment of the Burned Areas

Management of the burned areas resolves to three basic considerations. First, should the burned areas be covered with a dress-

ing? Second, if dressings are applied, should they be of the "pressure" type? Third, should the patient be treated with the open-air method? After many years of controversy over this aspect of the care of burned patients, a few basic principles are now better defined.

In some regions débridement of the burned surfaces is immediately performed and followed by dressings of petrolatum gauze covered by voluminous "pressure" dressings. We believe these practices are ill-advised on several counts. First, additional trauma of débridement is deleterious to the severely burned patient fighting a serious battle against shock; second, "pressure" dressings do not prevent edema. Recent studies by Price and colleagues have shown that local chilling to burned areas is the only known method whereby interstitial edema in the burned area can be lessened. When large quantities of Evans blue dye (20 mg. per kilogram of weight) were injected intravenously into dogs, and the animals then subjected to standardized burns, a staining of the tissues surrounding the burned area occurred within two minutes after receipt of the burn. The more intense the heat and the more prolonged the exposure, the wider became the zone of staining owing to edema and increased capillary permeability. For five minutes the tissue staining increased rapidly and then progressed more slowly over a 24-hour period. Pressure did not inhibit the escape of dye into or around the burned area, but immediate chilling did. Cold applied within 60 seconds and maintained for 10 to 15 minutes effectively reduced the escape of dye into the burned tissues.[26]

In 1949, when Rhinelander studied the tissue pressures between burned skin and a snugly applied plaster cast, he found an increase in pressure approaching, but never exceeding, mean arterial blood pressure. Edema developed proximal to the site of application of pressure, and the losses of circulating fluids were not lessened by the tight pressure cast. He concluded that any benefit to be derived from a "pressure" dressing would be in terms of a splinting effect only.[38]

During recent years we have had excellent results from the completely "open method" of management of patients with serious burns at both the University Hospitals and the Minneapolis General Hospital. When the acutely burned patient arrives at his hospital room, he is immediately placed on sterile sheets, with a large body cradle spanning the bed; the cradle is then draped with sterile sheets. Sterile technique about the bedside is maintained by everyone attending or visiting the patient. Temperature of the room is brought to approximately 80 F, and moisture added with a cold vapor humidifier. Nothing further is done to the areas of burned tissue at this time.

Patients arriving at the University Hospitals four or more days after the burning incident, and swathed in bulky "pressure" dressings, invariably have a foul, infected, and macerated exudate over the burned areas. Many patients are septic and toxic from growth of anaerobic organisms under these conditions. Upon removal of the foul dressings and exposure of the burned areas to the air, an immediate drying of the exudate results, and the patient becomes less toxic; he is more comfortable, has less pain, and his morale usually starts to improve. The Bradford-type frame serves usefully in the care of patients with circumferential burns of the torso or trunk. By turning the patient every two hours, a dry eschar soon forms over the burned areas. In all instances this eschar, when kept dry and intact, goes on to natural separation from underlying viable tissues from about the 14th to the 21st day after burn. Figure 2 demonstrates an eight-year-old girl about to be surgically débrided on the 15th day after burn. The dry character of the eschar is evident, and a tendency toward spontaneous separation from viable tissues is noted about the shoulders. This child received autografts and homografts immedi-

Fig. 2.—An 8-year-old child with third-degree burns of 65% of her skin treated without dressings of any kind at the University Hospitals. She is about to be débrided surgically on the 18th day after burn. Note the spontaneous separation of the dry, crusty eschar about the shoulders and arms.

ately after débridement, to 70% of her body surface.

Occasionally, in patients with very deep full-thickness burns, suppuration develops beneath the eschar and is heralded by signs of sepsis, high-spiking fever, and signs of toxicity. Eschar, under these conditions, must be opened, and drainage effected. Frequently this can be done painlessly and with facility in the bedroom. Depth of burn, however, is difficult to assess, and death of tissue sometimes extends into fascial spaces, tendon sheaths, joint spaces, and muscle planes. Burns of this extreme depth should be surgically débrided formally in the operating room as soon as sepsis is evident. Poor demarcation between viable and nonviable tissues and serious contamination with virulent bacteria contraindicate the application of split-thickness grafts at this first débridement in these circumstances.

Plan of Grafting of Full-Thickness Burns

When the eschar of the burned area is kept dry, natural separation begins about the 14th to the 21st day after burn. At this time we anesthetize the patient and, with a minimum of cutting necessary, dissect and strip the eschar off all areas to be covered by either homografts or autografts. The freshly denuded areas are washed with detergent and rinsed with saline. This viable recipient "bed" is in its most ideal condition for optimum "take" of split-thickness grafts. Autografts are used to the fullest extent possible, especially in flexion areas, about the face and neck, and on the hands. All

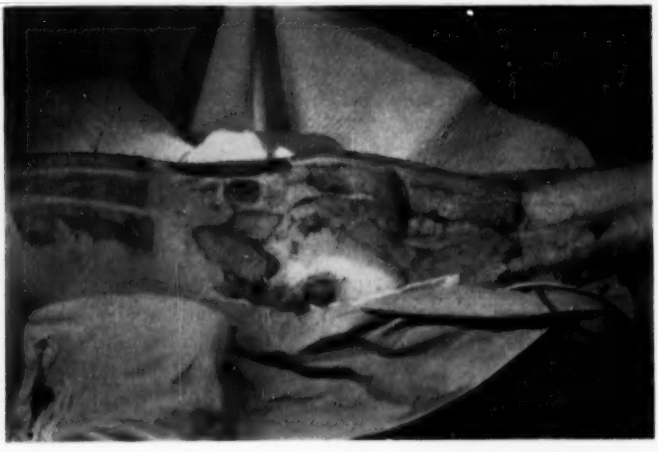

Fig. 3.—In patient at the Minneapolis General Hospital the autografted skin over the buttocks and thighs has healed 100% without dressings of any kind. Note cleanliness of the area on the eighth day after grafting when this picture was taken.

remaining freshly denuded areas are covered with homografted skin. If dressings are used, they are kept in place for only four or five days—and removed. Sepsis is rarely a problem under these conditions.

Following the work of Holman and associates in 1954, wherein the value of open-air healing of autografted skin was demonstrated in pigs, we have used the principle of no postoperative dressings on several burned patients and have had excellent results. Figure 3 portrays a General Hospital patient, aged 41, on the eighth postoperative day after application of eight drums of autografted skin to the buttocks, perineum, and thighs. Thirty per cent of the skin surface had been burned to a depth requiring grafting, and the dry eschar was removed at surgery, and the autografts taken from the abdomen and back. The skin grafts were tacked to the edges of the defects with 00000 nonabsorbable surgical sutures, and a dry dressing applied for only the first two postoperative hours while the patient was waking up. She was then placed on her abdomen on a Bradford frame, and all dressings removed. The grafts were not disturbed, and the cleanliness of the wounds and the completeness of the "take" are well demonstrated in the photograph taken on the eighth postoperative day. This patient was up and about ready to leave the hospital six weeks after her accident.

Figure 4 demonstrates a six-year-old boy partially covered with autografts and homografts at surgery on the 20th day after burn. Following a 50% body burn of third-degree depth, the patient was treated without dressings of any kind. The dry crusty eschar was removed on the 20th day after the trauma with a minimum of sharp dissection necessary. After washing the raw surface of the denuded burn bed with hexachlorophene (pHisoHex) and rinsing with sterile saline, autografts were taken from the back and placed about the neck and shoulders. Homografts were used over the chest and abdomen, with 00000 nonabsorbable surgical sutures used to anchor the grafts at the corners and at intermediate points along each edge. Both arms were suspended from a simple orthopedic framework over the bed, thick, soft pads being used about the wrists and lower forearms. The photograph taken on the seventh day after grafting indicates the remarkable cleanli-

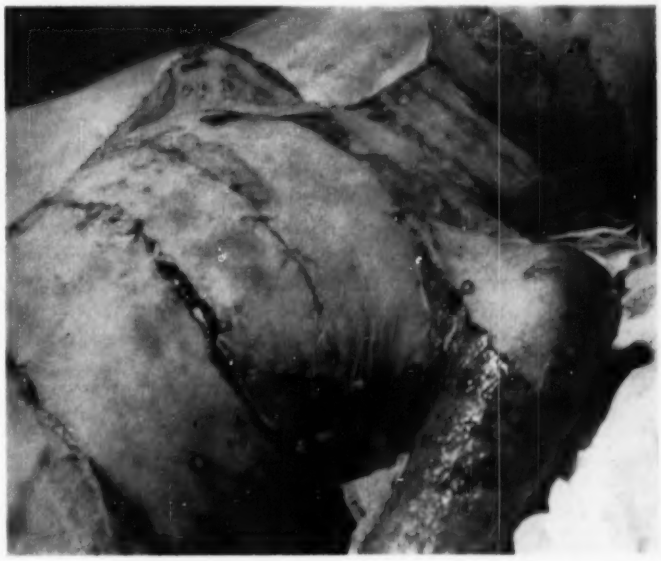

Fig. 4.—This 6-year-old patient at the University Hospitals was grafted with auto- and homografts immediately following débridement on the 20th day after burn. No dressings were used at any time. "Take" of the grafts was 100%, and the freedom from infection is noteworthy.

ness of the areas and the complete freedom from suppuration. The skin, both autografted and homografted, "took" about 100%.

We have never been able to cleanse adequately a denuded burn area, or an area of granulation, to the degree that suppuration would not immediately ensue following application of a bulky dressing creating anaerobic conditions. Many skin grafts are undoubtedly lost or severely damaged by lysis of the tissue from bacterial enzymes present under bulky dressings after three or four days. Serum from the recipient surface tends to "cement" skin grafts in place within a few minutes after they are applied. Healing and good "take" of the grafted skin will result if only gross sliding of the grafted skin is prevented. Smaller residual areas of granulation tissue have responded well to open-air management of this kind, when moist saline dressings have been applied three times daily to these regions. These "soaks" remain in place for only one hour.

Nutrition

A daily caloric intake far in excess of normal requirements is needed to offset the inordinate chronic depletion present during the postburn period. Severely burned adults require 4000 and 5000 calories daily. Commonly we have used gavage supplements for the poorly cooperative patient, and in our hands a mixture of puréed meats and vegetables in homogenized milk has proved highly satisfactory. In addition, 1 liter of rich eggnog made with cream and milk (half and half) will provide approximately 1500 calories. Natural foods have been better tolerated by our patients than protein hydrolysates of various kinds.

Daily recording of the caloric intake is essential, and one day below required intake should occasion real concern and cooperative remedial action among the physicians, nurses, and patient. Most patients, even the more stubborn and recalcitrant, will quickly exert the necessary effort to raise their natural oral intake high enough to be spared the gavage tube. Nowhere is the "art" of nursing more important than here; constant, cheerful, and persistent encouragement by the nursing staff usually suffices to accomplish the intake of needed calories entirely with oral feedings.

Summary

From 1945 to 1955 there were 170 patients treated at the University of Minnesota Hospitals for burns or problems associated with burns. There were 139 patients with third-degree burns in this group and 31 patients with burns of only first and second degrees. A total of 385 skin-grafting procedures were performed, and 64 additional operations were performed for complications and sequelae of the burned state.

The mortality among the 31 patients with first- and second-degree burns was 9.7%. These deaths were all in infants under one year of age. In the group of patients with third-degree burns, there were 17 deaths, or a mortality of 12.2%. The over-all mortality for the 170 patients was 11.7%.

When the patients with third-degree burns were divided into groups according to the per cent of body surface burned, it became apparent that there was a significant number of survivors in the more extensively burned group. There were five survivors of 40% burns, two survivors of 50% burns, two survivors of 55% burns, and one survivor of a 70% burn. However, in the group of 10 patients with 50% or more of their body surfaces burned to a depth of third degree, there were five deaths, or a mortality of 50%. The over-all mortality for all patients with third-degree burns of 15% or more body surface was 20.5%. This figure compares closely with a recently published figure by Moyer, indicating a mortality of 23.8% for a group of 315 patients with burns involving 15% or more of the body surface.

An analysis of the 15 deaths in patients with third-degree burns covering 15% or more of their body surface revealed a somewhat higher mortality in the extremes of life. Only two deaths were attributed to a state of shock, and both of these patients were in the infant group. Infection was a major cause of death in 4 of the 17 patients, and it was a contributing factor in 1 additional patient. The importance of a reduction in the rehabilitation phase of the problem in the burned patient is emphasized. The necessity of reducing the extensive protein drains upon the body and of reducing the period of time during which the liver is subjected to various injurious circumstances is discussed.

During recent years it has become evident at the University Hospitals and also at the Minneapolis General Hospital that the formula for electrolyte, fluid, and colloid replacement, as published by Evans and Purnell in 1952, has been most effective in our hands. The recently popularized plan of replacement therapy by the Brooke General Army Unit has proved to be somewhat high in electrolyte replacement. Our current replacement program calls for colloid solutions in the amount of 1 cc. per 1% of body surface burned per kilogram of weight (one-third to one-half of this amount to be given as whole blood), electrolyte solution of 0.75 to 1 cc. per 1% of body surface burned per kilogram of weight, and dextrose in water of 1000 to 2000 cc. A classic picture of water intoxication was encountered at the Minneapolis General Hospital in a severely burned patient receiving no electrolyte solution at all during the first 24 hours of replacement therapy. The relationships of the circulating plasma concentrations of electrolytes in this patient are presented. This patient had a serum sodium of 110 mEq. per liter 24 hours after receiving her trauma. Hypertonic saline, when given immediately in this circumstance, reversed the situation, and the patient recovered from her water intoxication. The necessity of providing a well-balanced fluid and electrolyte replacement program has been emphasized, and, in addition, the dangers of overtreating burned patients with excessive amounts of sodium have been discussed.

In the treatment of the burned area itself, our experience has indicated the value of a completely open method of management without recourse to initial débridement or cleansing of the burned areas. Approximately three weeks after injury, when the eschar begins to separate spontaneously from the deeper, viable tissue, débridement and immediate grafting with both homo- and autografts have been highly successful in our hands. Several patients are presented, demonstrating the excellent "take" and cleanliness of grafted areas seven and eight days after grafting when no dressings of any kind are used. The problem of earlier and more complete and definitive covering of the seriously burned patient with grafted skin is discussed. At the present time the efforts of all personnel involved in the care of the seriously burned patient should be directed toward the elimination of unnecessary delays in accomplishing the earliest and most complete grafting of the burned surfaces.

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Rokitansky-Aschoff Sinuses as a Presumptive X-Ray Sign of Gall Bladder Disease

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The presence of outpocketings of the gall bladder mucosa communicating with the lumen has been described by pathologists for almost 100 years. There has been considerable confusion concerning the histologic appearance, the mode of formation, and the pathologic significance of these pockets.

Rokitansky-Aschoff sinuses or cystitis glandularis proliferans refer to gall bladder diverticula. These protrusions of gall bladder mucosa through the muscular layer of the wall result from a weakness of the muscular layer together with an increased intraluminal pressure. Absence of a muscularis mucosa, sparseness of muscle fibers, and frequent piercing of the muscularis by blood vessels create the potential spaces for herniation of mucosa under the influence of disease. Inflammatory disease and increased intracystic tension from obstruction or neurogenic dysfunction are conditions which favor the occurrence of herniation.

These diverticula occur frequently, as demonstrated by Robertson and Ferguson,[1] who found them in half of the surgical specimens studied in patients over 30 years of age. Halpert[2] has noted that gall bladders with diverticula also show histologic evidence of chronic cholecystitis. He feels that these diverticula, when present on x-ray examination, indicate the existence of gall bladder disease.

Report of a Case

A 22-year-old white housewife was admitted to Meadowbrook Hospital on Aug. 28, 1954, with an eight-year history of postprandial distress. She had had frequent recurrent attacks of right upper quadrant pain following the ingestion of fried foods. These attacks were often associated with emesis, and the pain would radiate to the epigastrium and to both scapulae. Roentgenograms of the gall bladder performed four years prior to this admission revealed an elongated gall bladder, approximately 1 cm. in width (Fig. 1). Surrounding the narrow lumen were collections of dye which did not seem to communicate with the lumen. They were not present on the preliminary films. There was no evidence of cholelithiasis. A subsequent study four years later revealed essentially similar findings, with the exception that the collections of dye outside the surrounding lumen were not seen at this time (Fig. 2). Admission physical examination and laboratory studies were noncontributory.

Fig. 1.—Cholecystogram of June 1, 1950, showing constriction of the distal portion of the gall bladder with collections of dye about the narrow lumen. They represent visualization of the sinuses of Rokitansky and Aschoff. A biliary calculus is not seen.

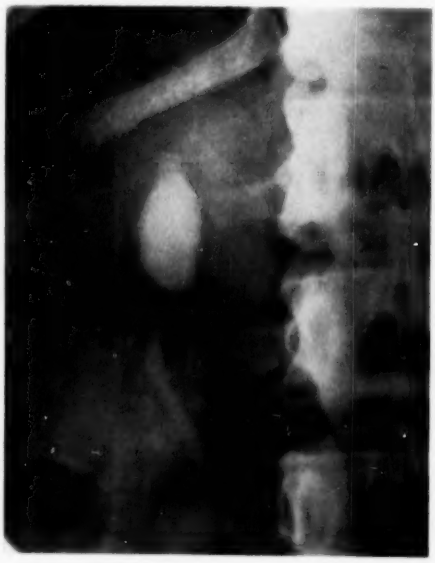

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Fig. 2.—Cholecystogram of June 17, 1954, showing changes similar to those in the preceding study. The diverticula do not visualize as well on this examination.

Since the patient had had the clinical symptoms of chronic cholecystitis during the intervening years, it was decided to perform a cholecystectomy. The gall bladder was thickened and fibrotic. There were a moderate number of adhesions between the gall bladder, the transverse colon, and the duodenum. The common duct was normal in size and consistency, and the cystic duct was not dilated.

The gross examination of the surgical specimen revealed the gall bladder wall to be 1 cm. in diameter. The wall was grayish white in color and moderately soft. A narrow lumen was found, which was filled with green bile containing many yellow stones, measuring approximately 0.2 cm. in diameter.

Microscopically there were pools of lymphocytes in the gall bladder wall. Many dilated cyst-like spaces were noted within the wall. These spaces were lined with gall bladder epithelium. Chronic cholecystitis was present (Fig. 3).

The patient had an uneventful convalescence and was discharged on the seventh postoperative day. A clinic visit nine months later revealed that the patient was completely free of symptoms.

Comment

A study of the cases of King and MacCallum [3] and of Ross and associates [4] reveals that the concentration of the dye and the visualization of the gall bladder were fairly good in each instance. The microscopic diagnosis of chronic cholecystitis was made in each case. In many of these cases, as well as in our own, the gall bladder contracted after a fatty meal. Ovbiously,

Fig. 3.—Histologic section of the gall bladder wall, showing a projection of mucosa lined diverticula into the muscular wall of the gall bladder.

the pathology present was not sufficient to prevent visualization of the gall bladder and postfatty meal contraction, both findings ordinarily being absent when cholecystitis exists.

It is also interesting to note that the diverticula in our case visualized without the necessity of resorting to a fatty meal. It must be assumed that the size of the duct entering the diverticulum was of sufficient size to permit easy entrance of the dye. In many cases where the diverticula do not appear until the fatty meal is administered, the ducts are presumed to be of a small caliber, and an increase in the intracystic tension is required to bring about visualization on x-ray examination.

In a number of cases in the literature a proximally located stenosis in the ampullary region of the gall bladder has existed. Stenosis was thought to play an indirect mechanical role in the visualization of the sinuses by producing a rise in the intracystic tension of the gall bladder, thus forcing the dye into the wall of the gall bladder. In our case the stenotic area was in the fundus of the gall bladder, with an area of apparently normal function in the ampullary region above the stricture. Under the circumstances it seems unlikely that the stricture would influence intracystic tension.

Summary

The anatomy, pathologic development, and appearance of gall bladder diverticula on cholecystography are described. The constancy of chronic cholecystitis in these gall bladders is mentioned.

It is apparent from a study of the cases in the literature, as well as our own case, that those gall bladders which reveal diverticula on cholecystography are usually accompanied by the signs and symptoms of chronic cholecystitis. In those cases in which a surgical specimen is obtained, the clinical impression is supported by the pathologic findings. It is evident then that these roentgenographic findings should be considered as strong presumptive evidence of gall bladder disease, probably equal in value to the well-known x-ray signs of nonvisualization and demonstrable calculi.

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Etiology and Treatment of Urinary Stress Incontinence in Women

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Urinary stress incontinence is far more frequent than has been realized, and as a result it has not received the attention it deserves. Even in mild cases stress incontinence is a social handicap. It is offensive to a fastidious woman and makes her constantly apprehensive, and so she is grateful for relief from the ever-present insecurity. Happily, normal function can be restored by means of present-day surgical techniques, and women do not have to go through life coping with this affliction.

The prevalence of stress incontinence was illustrated by a study made by Nemir and Middleton in 1954. They submitted a questionnaire to 1327 freshman women in the University of Utah, of whom 95% admitted having some stress incontinence. Of these only 5% experienced frequent loss, and none manifested any neurological or anatomical disturbance which would affect urinary control.

In our own series of 2063 gynecological cases covering 12 years, the records show that 309 patients complained of urinary stress incontinence, although it was clearly present in significant degree in only 262 cases. Some women are reluctant to admit that they are incontinent, and it is often difficult to establish the time of onset. Stress incontinence also is not necessarily constant, the histories showing many inconsistencies.

Because of the inconsistencies expectant treatment may be justified, unless the condition becomes too annoying to be ignored. Nonsurgical treatment may be helpful, but usually surgery is required for cure. Certainly these patients should have a thorough physical and urological examination before the type of treatment is finally selected.

Mikuta [1] in 1953 listed in detail the many causes of urinary incontinence, which may be summarized as follows: congenital anomalies of the urinary tract; lesions of the nervous system; tumors; calculi; trigonal hernias; chronic urinary infections; inflammatory or neoplastic masses of genital or intestinal origin; urinary fistulas; pregnancy; childbirth injuries; surgical scars and adhesions; uterine prolapse; cystourethrocele, and occasionally even enterocele.

A severe chronic cough may precipitate or increase stress incontinence, especially if sphincter weakness is already present, but it is possible for the patient to improve voluntary control with practice. Incomplete emptying of the bladder may be a factor, as well as the patient's constitution, temperament, and general health. Some women fail to make sufficient effort to control the urine by using the voluntary muscles of the pelvic floor. Others exaggerate their condition, and examination reveals only negligible incontinence. Incontinence varies from time to time, increasing when the patient is especially nervous or tired. Diseases, such as diabetes, which cause an excess flow of urine also may increase incontinence.

Anatomy and Physiology of Bladder and Urethra

Through the years opinions have differed greatly with respect to the anatomy and functioning of bladder and urethra, the defects involved in urinary incontinence, and the best methods of overcoming these defects. The fibers of the various struc-

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tures are so intimately intermingled that definitive dissection is difficult. Consequently, a complete and detailed picture of the urinary tract seems to be unavailable. We can only outline our impression of the present-day concensus gleaned from a considerable cross section of the literature.

The basic support of the pelvic viscera is provided by the pubococcygeus muscles and the urogenital diaphragm. These structures are pierced by the urethra and vagina and contribute fibers to their walls. The walls of bladder and urethra are lined with mucosa and are composed mostly of three layers of smooth (involuntary) muscle fibers, with some intermingling of striated (voluntary) fibers. The inner and outer layers are longitudinal, and the middle layer is circular or spiral. There is an outer sheath of fascia.

Three urethral sphincters have been described—external and central sphincters of striated muscle and an internal sphincter of smooth muscle. In some specimens the outer sphincter is missing, but in other specimens it has been cleanly dissected from around the external meatus. The central sphincter is missing from many specimens, and its derivation is uncertain. The upper sphincter, which surrounds the internal os, is made up of two horseshoe-shaped loops of smooth muscle, one arising in the anterior wall of the bladder and the other in the posterior wall, with the ends of each inserted in the opposite wall. They close the urethra by apposition of the anterior and posterior walls. The lower loop, which draws posteriorly, is much heavier and less mobile than the upper loop, which draws anteriorly. This may be partly compensated for by the interdigitation of the pubovesical muscles and ligaments with the bladder musculature to the periphery of the anterior loop. Contraction of these ligaments aids in closing the os, while relaxation permits it to open.

The urethral submucosa (corpus spongiosum or venous pads) is made up of a loose connective tissue which contains a highly developed system of venous plexuses and is cavernous in character. Distention of the bladder narrows the venous lumina in its wall, producing congestion in the capillaries of the venous pads. This exerts pressure on the mucosal folds and aids the sphincters in snug closure of the internal vesical os.

The mechanism of urinary control, as visualized by Power,[2] is briefly as follows: The triangular shape of the empty bladder results from its attachment to the pubes, to the urachus, and to the uterus and vagina. As the bladder fills, it extends transversely, always maintaining a horizontal fluid level. When the bladder is filled, a reflex occurs which involves the involuntary musculature. The wall contracts; the pubovesical ligaments are stretched, leaving a gap of 1 cm. between symphysis and bladder. Resistance at the funnel-shaped internal vesical os is lowered. The os is pushed downward and backward, and fluid is expressed into the urethra, relaxing both sphincteric loops. Simultaneously decongestion of the venous pads occurs. Pressure from the urinary stream relaxes the urethral muscles, so that the canal is shortened and the posterior wall slides forward. When the bladder is empty, the process is reversed. Active control to maintain continence is a function of the levator ani muscles and the external striated sphincter, and relaxation of these muscles is necessary for normal micturition. The caliber of the stream can be increased, however, by downward pressure produced by contraction of abdominal muscles.

Students of the mechanism of continence believe that the backward and downward shifting of the internal os initiates micturition, and its automatic return to the physiological level is the key to continence. X-ray evidence suggests that the shifting and subsequent return depend on the relaxation and contraction of the levator ani muscles.

Stress incontinence, Power believes, is due to a momentary downward and backward displacement of the bladder, which relaxes the sphincteric loops by tension on the pubovesical muscles. Dribbling inconti-

nence, he suggests, may be caused by (1) a permanent downward and backward displacement of the bladder; (2) trauma to the smooth-muscle sphincters; (3) impairment of the nerve supply, or (4) possibly shortening of the pubovesical muscles. The external striated sphincter is used, in his opinion, only when the involuntary mechanism has broken down. It seems to us that relaxation or laceration of the pubovesical muscles would be a more likely cause of incontinence than shortening.

Jeffcoate and Roberts[3] (1954) stress the importance of the posterior urethrovesical angle. In the normal woman micturition obliterates this angle, but stress does not affect it. Even in the presence of uterine prolapse, loss of urine does not occur on stress, so long as the normal angle is preserved. In stress incontinence the most characteristic change is loss of this angle, so that the trigone and urethra tend to come into line. According to Ullery[4] (1954) the normal angle is 16 degrees, whereas in women with stress incontinence the angle varies from 0 to 10 degrees.

The most constant finding after a successful urethrocystopexy for stress incontinence, according to Jeffcoate and Roberts, was restoration of the posterior urethrovesical angle. A successful operation usually resulted in some uplift of the bladder base, but this was not a striking feature. Difficulty in micturition occurred especially when the urethrovesical junction was unduly elevated and immobilized, and appeared to be the result of extreme angulation of the urethra at the urethrovesical junction and narrowing of the urinary stream. Exaggerated uplift may also leave a pouch of bladder at the back which is never completely emptied. Undue fixation of the bladder base interferes with initiation of micturition, because it prevents the normal descent which triggers the micturition reflex.

It is obvious that a process so intricate as urinary control can be interrupted at any one of several points. Usually, although not always, stress incontinence is associated with cystourethrocele. The basic cause for both probably is damage to the pelvic floor, especially the pubococcygeus muscles. This damage permits involuntary downward and backward displacement of the bladder and internal os, which initiates micturition. Equally important is tearing, stretching, or relaxation of the pubovesical muscles and ligaments. These ligaments interdigitate with the internal sphincter and directly affect its function. Their relaxation also allows the urethra and bladder to sag, with loss of the posterior urethrovesical angle.

In view of these causes of urinary incontinence, it is not surprising that many cases can be relieved by correction of cystourethrocele. It is well to repair even small, early, asymptomatic cystoceles when other vaginal surgery is done. Given enough time, these are liable to develop into large symptomatic cystourethroceles, often with stress incontinence.

Nonoperative Treatment of Stress Incontinence

Kegel[5] and his associates found that many patients show atrophy of the voluntary muscles in the region of the vesical neck. This may have resulted from parturition, or it may have been present throughout life. They estimate that between 30% and 40% of all women lack normal muscle function and have little or no awareness of their ability to contract these muscles voluntarily. Kegel measured the strength of the muscle contractions by means of a perineometer and found that average pressure varied between 30 and 60 mm. of mercury, while those who were unaware of their ability to contract the muscles produced little or no increase in pressure.

On the basis that fascia, connective tissue, and muscle are strengthened by activity and weakened by continued static stress, Kegel devised exercises which he recommended that patients practice for

20 minutes three times a day. He found that 60% showed improvement; 6% relapsed after stopping the exercises, and no improvement was shown by 25%. Of patients whose incontinence persisted after vaginal surgery, 71% were relieved by the exercises. Best results were obtained when the exercises were continued for at least six months. This treatment is not intended to replace surgery, but, used in conjunction with it, better results were obtained. We believe that patients with mild cystourethrocele and stress incontinence, as well as those who have had only partial success with surgery, should try nonoperative treatment before surgery is recommended.

Urinary infections, of course, must be eradicated, and Rashbaum and Mandelbaum supplement specific treatment with exercises in repeated starting and stopping of the urinary stream.

Salmon has suggested estrogen therapy to overcome the genital atrophy which usually follows the menopause. Symptoms improve during treatment but recur after it is discontinued.

Surgical Treatment of Urinary Stress Incontinence

Ullery (1954) divided the operations for relief of stress incontinence into four groups and prepared detailed lists of dates, surgeons, and procedures included in each group. Even his study was not exhaustive, and the few examples outlined here serve chiefly to illustrate the complexity of the problem and the types of approach to its solution.

Urethral Advancement.—Pawlik [6] (1883) denuded an area on each side of the urethra and sutured the denuded surfaces in such manner as to stretch and elevate the urethra and advance the external meatus close to the base of the clitoris.

Between 1900 and 1946 nine other suggeons used variations of this technique, some of them with great success. Berkow [7] (1941) combined advancement of the urethra with paraurethral fixation, using the bulbocavernosus muscles for support. This proved to be one of the most important operations for relief of stress incontinence. Another noteworthy contribution was the operation of Ingleman-Sundberg [8] (1946) in which he used the pubococcygeus and ischiocavernosus muscles to support the advanced urethra.

Sling Operations.—Long the most popular type of surgery for relief of stress incontinence because usually they were successful, the musculofascial sling operations were nevertheless formidable procedures for both patient and surgeon. Twenty-two surgeons were listed in the group using this type of procedure, beginning with Giordano (1907) and ending with Millin and Read [9] and Marshall [10] in 1948. Each of these men developed a greater or lesser variant of the basic operation.

Most of the sling operations involved two incisions—one in the lower abdomen and the other over the urethra. Through the abdominal incision the gracilis or pyramidalis muscles were freed to use as slings, or one or two strips of rectus fascia, longitudinal or transverse, were freed except for a pedicle at the upper or outer end of each strip. Bilateral tunnels were made (either posterior or anterior to the pubis) between the abdominal and suburethral incisions, and a fascia strip was passed downward through one tunnel, then under the urethra, then returned to the abdominal incision via the other tunnel, to be anchored to the rectus fascia. Sometimes two strips were dissected, passed downward, and sutured together under the urethra. Fascia-lata slings occasionally were used in a similar manner.

Probably the most popular of the sling operations was that of Millin and Read (1948). Through a transverse lower-abdominal incision they dissected bilateral transverse strips from the anterior abdominal aponeurosis, extending about 3 cm. into the oblique muscles and pedicled on the muscles. Each strip was passed through the rectus muscle on the same side, then

under the urethra, and through the opposite rectus muscle. Finally it was turned back and sutured to the other strip in the midline. One advantage of this operation is that it requires only one incision. The results usually are good, but the technique is intricate, and postoperative difficulties with urination are greater than after many other operations, possibly because it is very easy to tear the urethra in tunneling under it.

As with advancement of the urethra, the most important result of all the sling operations was elevation of the urethra and restoration of the posterior urethrovesical angle—and these complex procedures did most effectively.

Plication Operations.—Kelly [11] (1911) appears to have been the pioneer in operations of this type. Through an anterior vaginal incision he repaired and plicated the torn or relaxed tissues of the vesical neck, then trimmed the margins of the vaginal flaps, and closed them snugly to support the urethra and bladder. Te Linde later suggested that if incontinence is associated with scar tissue from childbirth or previous surgery dissection should be carried two-thirds of the way around the urethra, leaving only its superior attachment intact, before plication is done.

Many other modifications of the Kelly operation were developed. One of the most radical of these was devised by Millin [12] (1939). He opened the bladder suprapubically and tightened the sphincter mechanism about the bladder neck with sutures in the trigone muscle and the internal sphincter of the urethra. Goldberger and Davids (1947) plicated and replicated the anterior vaginal wall, using a buried tantalum plate to lend additional support to the bladder neck and urethra.

Kennedy [13] (1937) introduced an operation which superseded the Kelly procedure in popularity. Through an anterior vaginal incision Kennedy (1) separated the bladder from the cervix, (2) freed the vaginal wall from the bladder laterally as far as the pubic rami and forward to within 1.5 cm. of the external meatus, and (3) separated the urethra from the median posterior margins of the rami out to the paravesical space. Midline mattress sutures plicated the fascia of the weakened posterior wall of the bladder, urethra, and trigone. Margins of the vaginal wall were trimmed, leaving a slight redundance. Three silver wire sutures then were placed through the vaginal wall on one side, passing very close to the margins of the pubic rami, picking up fibers of the levator ani muscles, and emerging through the vaginal wall on the other side. The vaginal wall was closed, and the silver wires were approximated, to remain in place until about the 12th day.

Perhaps the best of the plication operations is that of Te Linde [14] (1953), who uses it for repair of urethrocele with or without stress incontinence. His description of the operation may be summarized as follows: A midline incision is made through the vaginal mucosa, and the flaps of mucosa are dissected laterally. Mattress sutures are placed on each side of the urethra and parallel with it, beginning less than 1 cm. above the meatus and extending to the trigonal region and past the junction of urethra and bladder. The entire urethral tube, as well as the region of the internal sphincter, is thus tightened. As the sutures are tied, the tissue between them is inverted by an assistant who presses lightly over the urethra with a Halsted clamp. A second row of slightly coarser stitches is then placed through the pubovesicocervical fascia, outside of and parallel to the first row. After the second layer of plicating stitches has been tied, the excess of vaginal mucosa is excised, and the mucosa is approximated in the midline. This operation may be done alone or in combination with the operation for cystocele.

Our own plication operation for cystourethrocele is similar to that of Te Linde, although we would describe it differently. We start with an incision through both layers of the vaginal wall—the mucosa and the musculofascia. We separate the vaginal

fascia from the fascial envelope of the bladder and urethra and then from the vaginal mucosa. After plicating the fascia of the bladder and urethra, we close the vaginal fascia as a separate layer, imbricating any redundant tissue. The margins of the mucosal flaps are trimmed to fit the space, and the mucosa is closed. We feel that closure of the vaginal wall in two separate layers gives much better support to the bladder and urethra than closure in a single layer. This, we believe, is because each layer can be tailored more accurately to fit the space, and because imbrication of the vaginal fascia strengthens the wall and therefore lends better support to bladder and urethra than when it is merely coapted. After the repair is completed, a No. 28 urethral sound is introduced in order to assure a patent urethral canal. Five days later this may be repeated after the catheter is removed.

We have found that a well-executed plication operation will relieve urinary stress incontinence associated with cystourethrocele in a large proportion of cases. A survey of our 262 cases from 1942 to 1953, inclusive, reveals the following results: symptom-free, 198; improved, 35; unchanged, 10; worse, 3; recurred, 2, and not followed, 14. Thus, results in the primary cases were favorable in 89%, unfavorable in 5.6%, and unknown in 5.4%. Reoperation in the two recurrent cases resulted in cure. With the improved technique of recent years, we believe that the results have improved comparably. It may be of interest to add that, out of 2063 gynecological cases, stress incontinence was present in 1 of 8 cases (12.7%), and in the total of 649 cystourethrocele repairs stress incontinence was present in 1 of each 2.5 cases (40.4%).

Vesicourethral Suspension (Urethrocystopexy).—The first suprapubic approach to the problem of stress incontinence appears to have been made by Victor Bonney[15] (1923). He aimed to elevate the bladder neck and urethra and reestablish the posterior urethrovesical angle by tightening the fascial supports and lengthening or narrowing the urethra. He placed his sutures through the bladder wall, however, and unfortunately the wall stretched so that his good results were not permanent.

Various other operations having the same objective were reported during the next quarter-century, but none has been more successful than that proposed by Marshall, Marchetti, and Krantz,[16] especially after subsequent improvements in their technique were developed.

These surgeons placed in the bladder transurethrally a 30 cc. balloon attached to a Foley catheter and inflated the bag. With the patient in the Trendelenburg position, the space of Retzius was exposed through a midline suprapubic incision. The bladder and urethra were separated from the posterior surface of the pubis and the rectus muscles down to 1 cm. or less from the external urethral meatus.

Three No. 1 chromic absorbable surgical sutures were placed at equal distances on each side of the urethra, the suture needle being inserted deep into the anterior vaginal wall and through the lateral wall of the urethra. A double bite was then taken, to place as much tissue as possible in apposition to the pubes. The balloon was pulled down to mark the outlet, and a similar suture was placed between balloon and catheter. By upward traction on the long ends of these eight sutures, the urethra and vesical neck were lifted away from the introitus. The long ends of the sutures were placed in the periosteum of the symphysis, preferably in the cartilage, or in the rectus muscles if indicated. When tied, they moved the urinary passage upward and backward from the introitus. The space of Retzius was closed, and additional sutures were placed in the musculature of the lower and lateral portions of the bladder, with the long ends in the posterior aspect of the rectus muscles. These sutures drew the bladder anteriorly farther into the space of Retzius.

As a prognostic test before surgery, the bladder was filled with saline solution, then

a wheal of procaine hydrochloride (Novocain) was raised in the vaginal wall under the interureteric ridge. The area was grasped with an Allis clamp and held firmly upward while the patient coughed and strained. If elevation and fixation produced good urinary control, the test was considered favorable. Additional evidence was provided if pulling the vesical base downward toward the introitus caused poor control.

Marshall, Marchetti, and Krantz obtained cures in 74% and improvement in 18% of their early operations. The 8% of failures were ascribed to improper selection of patients. Results reported in the recent literature indicate cures in 90% to 95% of appropriate cases.

Of the many operations devised for relief of urinary stress incontinence, no other has the direct approach and the simple technique of the Marshall-Marchetti. We feel that this procedure has been greatly undervalued and that it is the most practicable as well as the most successful of the operations yet proposed. Our interest in it has grown with experience, and we have welcomed the opportunity to work with Irving Helfert, M.D., urologist, of Dayton, in developing our skill.

We are reporting on 44 cases. Of these, Dr. Helfert contributed 15, and we have added 17 of our earlier ones and 12 in which surgery has been done too recently for final evaluation, although the immediate results have been very pleasing. Dr. Helfert reports cures in 14 of his cases and failure in 1 case because of a postoperative hemiplegia. Of our earlier group, 13 patients are symptom-free, 2 are improved, and 2 are unimproved because of preoperative cerebral accidents. We have learned the hard way that such patients are not suitable candidates for urinary surgery.

Our technique differs from the original Marshall-Marchetti technique chiefly in that we do not insert our No. 1 chromic absorbable surgical sutures through the wall of the urethra. We pass them through the anterior vaginal wall lateral to the urethra, then attach them closely to the pubic periosteum. It is also desirable in some cases to place three or four sutures in the bladder wall, anchoring them to the rectus muscles. We try to avoid penetrating the bladder mucosa, although we do not always succeed. So far, in our experience, it has not caused any ill effects other than a little bleeding. Upward pressure on the anterior vaginal wall by an assistant with two fingers in the vagina facilitates the snug tying of the sutures. Two small rubber drains are inserted, and the abdominal wound is closed.

This procedure obliterates the space of Retzius, apposes the anterior surface of the urethra and bladder neck to the rami of the symphysis, and restores the posterior urethrovesical angle. It also provides support for the anterior vaginal wall and eliminates cystourethrocele.

Plication and vesicourethral suspension are not completely interchangeable. Each has its own place in the treatment of cystourethrocele and urinary stress incontinence, with loss of the posterior urethrovesical angle. For control of these conditions we prefer plication if the remainder of the procedure is vaginal. When the abdomen must be opened, however, vesicourethral suspension may be elected. Good results have been achieved with both techniques.

Summary

In the majority of cases cystourethrocele and urinary stress incontinence are related to obstetrical injury to the pelvic floor, often accompanied by tearing or stretching of the pubovesical muscles and ligaments. Damage to the floor may permit involuntary downward and backward displacement of the bladder and internal os, which initiates micturition. Momentary displacement produces stress incontinence; permanent displacement causes dribbling incontinence. When the pubovesical muscles are torn or stretched, there may be loss of the posterior urethrovesical angle, together with relaxation of the internal sphincteric loops—both related to incontinence.

The techniques proposed for correction of stress incontinence are classified in four groups: urethral advancement; sling operations; plication operations, and vesicourethral suspension. All these operations have in common the elevation of the urethra and restoration of the posterior urethrovesical angle, and some success has been achieved with most of the many techniques devised. For control, however, of cystourethrocele and urinary stress incontinence we prefer either a modified Te Linde plication or a modified Marshall-Marchetti vesicourethral suspension. The former usually is chosen when the entire procedure is vaginal; the latter may be elected when the abdomen must be opened for hysterectomy or other surgery.

Our 2063 gynecological cases, treated between January, 1942, and December, 1953, included 649 plications for cystourethrocele, 31.4%. Stress incontinence of significant degree was present in only 262 cases, or 40.4% of the plications and 12.7% of the entire series. Results were favorable in 89% of the 262 cases, unfavorable in 5.6%, and unknown in 5.4%.

Of the 44 vesicourethral suspensions reported, 12 were done too recently for final evaluation, although immediate results are excellent. Of the remaining 32 operations, 27 (84.375%) were successful; 2 (6.250%) produced improvement; 2 (6.250%) failed because of preoperative cerebral accidents, and 1 (3.125%) recurred because of postoperative hemiplegia.

Nonoperative treatment is useful in some cases before and after surgery to tone up the tissues, but it seldom can replace surgery.

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Acute Perforated Diverticulitis of the Sigmoid Colon with Generalized Peritonitis

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Acute free perforation of a diverticulum of the sigmoid with generalized peritonitis is a rare complication of diverticulitis. Arnheim [1] in reviewing 834 cases of surgically treated diverticulitis from the literature found that 19% of cases had abscess formation, 12% had localized peritonitis, and only 2% had spreading peritonitis. The very nature of the inflammatory process in diverticulitis of the sigmoid is in essence a peridiverticulitis. This promotes dense adhesions to surrounding structures, such as small bowel, bladder, cecum, and other segments of sigmoid at an early phase in the inflammatory process, with resultant abscess and fistula formation but rarely with free perforation to the peritoneal cavity with generalized peritonitis.[2] Maingot [6] states that the seriousness of this rare complication of diverticulitis requires prompt surgical definitive intervention in order to lessen the high mortality rate from such a lesion. At the Riverside Medical Clinic in the past five years we have encountered four patients with free perforation from diverticulitis who presented themselves as having typical clinical pictures of acute spreading peritonitis. In only one instance was a preoperative diagnosis of the true pathology correctly made. At surgical exploration in two instances a perforated appendicitis was suspected, and consequently a lower right rectus incision was made. The actual pathology was easily located and treated without difficulty in each instance by the right rectus approach. In two patients the more expedient left lower rectus incision was used because of predominantly left-sided signs and symptoms in one case and a correct preoperative diagnosis in the other case.

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The Riverside Medical Clinic.

Report of Cases

CASE 1.—A 36-year-old man was well until one week prior to admission, when he noted mild lower abdominal cramping pains relieved by bowel movements and passing gas. Twenty-four hours prior to admission the lower abdominal pains became severer and seemed to be localized in the midline suprapubic area. In spite of this, the patient went out to dinner and ate a large meal, after which he felt rather distended and had a constant urge to urinate. During the next 12 hours the pains became progressively severer, and there was an associated frequency but no dysuria, hematuria, pneumaturia, or pyuria. Six hours prior to admission the patient gave himself a tap-water enema, and, being somewhat relieved, he repeated this procedure. Before he could expel the second enema, he became very weak and nauseated. After this, the pains became very severe, requiring the patient to lie still for relief. Movement accentuated the pain, and he felt best with his knees flexed. Two hours before admission the patient's temperature was 100.6 F orally. There was no history of recent change in bowel habits or melena. The past history was negative, as was a careful review of systems. There was no history of recent weight loss.

On admission to the hospital, physical examination revealed a rather obese, stocky, white man acutely ill with obvious abdominal distress. His knees were drawn up on the abdomen. The physical examination was otherwise negative except for the abdomen, which was moderately protuberant and distended, with generalized lower abdominal tenderness most marked in the suprapubic area and right lower quadrant. There was associated rebound tenderness to the right suprapubic area and mild right lower quadrant rigidity. Bowel sounds were diminished. There were no palpable masses. There were no positive findings in the upper abdomen, and the liver, kidneys, and spleen were not palpable. Rectal examination re-

vealed no definite masses but exquisite tenderness in the suprapubic and right lower quadrant areas.

The laboratory studies on admission showed erythrocytes, 5,400,000; hemoglobin, 16.2 gm., and leukocytes, 26,800, with 76% segmented forms and 2% stab forms. Urinalysis showed no albumin, sugar, or acetone, and the microscopic examination showed no leukocytes, erythrocytes, pus cells, or casts. The specific gravity was 1.005. The N. P. N. was 39 mg. per 100 cc.; the CO_2 was 27 mEq. per liter, and the serum chlorides were 98.4 mEq. per liter.

A preoperative diagnosis of an acute surgical abdominal condition, most likely appendicitis, was made, and on Nov. 15, 1954, through a lower right rectus incision the peritoneal cavity was opened. A moderate amount of cloudy peritoneal fluid with a fecal odor was encountered, extending to all quadrants of the abdomen. The appendix was normal, and the pathology was found to consist of a segment of distal sigmoid, 15 cm. in length, densely indurated and inflamed, partially adherent to the dome of the bladder. This segment of sigmoid lay almost in the midline, and spillage of fecal material was predominately into the right peritoneal gutter. This explained the patient's right-sided symptoms and signs. At this point there was an open perforation of the sigmoid, 1 cm. in diameter, through which air and liquid fecal material were escaping to the free peritoneal cavity. The colon above and below this involved segment appeared normal. Therefore, an anterior resection of the lesion was performed with an end-to-end anastomosis. An indurated small segment of the bladder at the point of adherence was excised, and the bladder wall was closed. Gross and frozen-section pathological examination showed the lesion to be a perforated diverticulitis. There was no evidence of malignancy. The patient received intravenously 500 mg. of oxytetracycline (Terramycin) every 12 hours for 3 days postoperatively and made an uneventful recovery and has remained well to the present time.

Case 2.—A 51-year-old man was well until 48 hours prior to hospital admission. Four days prior to admission he fell off a chair in his office, hitting his head and sharply twisting his abdomen. He was asymptomatic from the accident until 24 hours later, when he developed left lower quadrant, nonradiating pain after a bowel movement. This persisted, becoming progressively severer over the next 36 hours, after which the patient was admitted to the hospital. There was no history of recent change in bowel habits or melena. For 12 hours the patient had noted marked nausea and anorexia but no vomiting.

On physical examination the temperature was 100.2 F; the pulse was 88, and the respirations were 18. The patient appeared to be in acute abdominal distress. There was marked tenderness over the entire lower abdomen, most pronounced in the left lower quadrant. This was associated with left lower abdominal rigidity and rebound tenderness. Bowel sounds were absent. There was no costovertebral angle tenderness. Rectal examination showed left lower quadrant tenderness. There were no palpable masses. The remainder of the physical examination was essentially negative.

Laboratory examinations showed the erythrocytes to be 4,450,000 with 16.2 gm. of hemoglobin. The leukocyte count was 24,000, with 72% segmented forms and 20% stab forms. The urinalysis was negative. A diagnosis of acute surgical abdomen, most likely appendicitis but possibly perforated diverticulitis, was made, and on May 24, 1956, through a left lower rectus incision the peritoneal cavity was opened. A large amount of cloudy, purulent fluid was encountered with a fecal odor extending to all quadrants of the abdomen. The appendix was normal. On inspecting the sigmoid, the site of pathology was quickly encountered as an inflammatory perforating lesion of the midsigmoid with a densely adherent loop of ileum attached to it. There was a free opening, 0.8 cm. in diameter, from the sigmoid into the peritoneal cavity at this point, through which were escaping gas and fecal material. An anterior resection of the indurated inflamed sigmoid, a segment of 12 cm. in length, was performed with an end-to-end anastomosis. The inflamed adjacent midileum was similarly tangentially excised and closed.

Postoperatively the patient received intravenously 500 mg. of oxytetracycline every 12 hours for 3 days. He made an uneventful recovery and has remained well to date.

Case 3.—A white 68-year-old woman was first seen one week before admission with left lower quadrant, nonradiating abdominal pain, a slight increase in constipation, and some mild abdominal bloating. There was no history of melena, and the physical examination was negative except for a temperature of 99.6 F and very mild left lower quadrant abdominal tenderness. A barium enema was performed, which revealed a stenosing lesion in the distal sigmoid area. The radiologist could not differentiate carcinoma from diverticulitis in this instance. After the barium enema the pain had become severer, and while the patient fortunately had satisfactorily evacuated the barium, she had noted more constipation since the barium enema. The patient was referred to me for proctoscopic examination, as the nature of the lesion was as yet undetermined. On June 16, 1956, a sigmoidoscopic examination was performed, the instrument being introduced with ease to 24 cm. At this point there seemed to be some spastic narrowing of the sigmoid, but no mucosal

pathology was seen. Ten hours after this examination the patient called me, stating that her left lower quadrant pain was much severer and that, in addition, she was having bilateral shoulder pain increased on deep breathing. Examination revealed increased tenderness in the left lower quadrant with associated rigidity and rebound tenderness. The patient was admitted to the hospital where a flat plate of the abdomen showed air under both diaphragms. The erythrocyte count was 4,250,000 with a hemoglobin of 14.6 gm. The leukocyte count was 18,250, with 71% segmented forms and 10% stab forms. The urinalysis was negative.

A diagnosis of perforated diverticulitis with spreading peritonitis was made, and the abdomen was opened through a left lower rectus incision. On opening the peritoneal cavity, a large amount of gas escaped. Examination of the sigmoid colon showed a discretely inflamed and indurated diverticulum of the midsigmoid, about 25 cm. above the peritoneal reflexion of the rectum. The diverticulum was 2.5 cm. in diameter at its tip, through which air and fecal material from the colon were slowly escaping. The sigmoid adjacent to this diverticulum was surprisingly free of inflammation. There had been no attempt on the part of this inflammatory lesion to become adherent to other structures in the abdomen. There was extensive diverticulosis of the remainder of the sigmoid, but all other diverticula were less than 0.5 cm. in size, and none showed inflammatory reaction. Because of the nature of the discretely localized pathology here, the diverticulum was merely excised with a small margin of normal sigmoidal wall, and the sigmoid was then closed. Postoperatively the patient received 500 mg. of oxytetracycline administered intravenously every 12 hours for 72 hours and has made an uneventful recovery to date. It is interesting to note that her left lower quadrant pain has disappeared, as has her preoperative low-grade fever.

CASE 4.—A 63-year-old white man was well until five days prior to hospital admission on Feb. 10, 1955, when he noted a gradual onset of lower midabdominal cramping nonradiating pain. The bowels moved daily with laxatives, and there was no history of recent change in bowel habits or melena. Eight hours before admission, the patient had a mild chill; the pain became severer, and he vomited once. He had exhibited marked anorexia and nausea for 12 hours prior to admission. There were no urinary symptoms and no evidence of recent weight loss.

The past history was negative except for syncopal attacks due to an A. V. block of varying degree one year previously and a transurethral prostatectomy performed five years previously.

On admission to the hospital, the patient, except for a flushed face, did not look acutely ill. The physical examination was negative except for moderate obesity, auricular fibrillation, and mild clubbing of the toes but not the fingers. Abdominal examination revealed moderate lower abdominal distention in a soft protuberant abdomen. There was questionable rigidity in the right lower quadrant with marked tenderness over the entire hypogastrium, most marked in the right lower quadrant and midline suprapubic area. Rebound tenderness was marked in the right lower quadrant. Bowel sounds were hyperactive. No masses were felt. There was no costovertebral angle tenderness. On rectal examination the prostate gland was small, and there was no abdominal tenderness. The patient had bilateral inguinal herniae which were easily reduced. The temperature was 100.4 F; the pulse was 104; the respirations were 20, and the blood pressure was 140/92. Pulsations were readily palpable in all vessels in both extremities.

Laboratory studies at this time revealed 5,500,000 erythrocytes, 15.7 gm. of hemoglobin, and 18,800 leukocytes, with 20% stab forms and 71% segmented forms. The urinalysis was essentially negative except for 15-20 pus cells per high-power field and numerous bacteria. A scout film of the abdomen showed no free subdiaphragmatic air and an intestinal pattern suggesting paralytic ileus. An intravenous pyelogram showed normally functioning kidneys without evidence of disease and no evidence of ureteral calculus as obstruction. Eight hours after admission all abdominal signs seemed increased in severity, and bowel sounds appeared diminished. The leukocyte count remained unchanged.

Abdominal exploration was performed through a lower right rectus incision with a preoperative diagnosis of "acute surgical abdomen," most likely acute appendicitis. Upon opening the peritoneal cavity, a large amount of purulent fluid was encountered in all quadrants of the peritoneal cavity. The appendix was normal, and an uninflamed Meckel's diverticulum was found in the ileum about 25 cm. from the ileocecal valve. The primary pathology was noted to be present in the lower sigmoid, 15 cm. above the peritoneal reflexion; it consisted of a densely indurated and inflamed segment of sigmoid, 10 cm. in length, with a central free perforation, 1 cm. in diameter, through which gas and fecal material were escaping. There was no evidence that an attempt had been made by surrounding structures to wall off this opening. The adjacent sigmoid and rectosigmoid appeared normal. Therefore, it was elected to proceed with a primary anterior resection of the involved segment of sigmoid with an end-to-end anastomosis, which was performed without incident. Pathologic examination of the tissue removed showed perforated diverticulitis. The

Meckel diverticulum was then excised tangentially from the ileum which was closed. The appendix was not removed.

Postoperatively the patient received intravenously 500 mg. of oxytetracycline every 12 hours for 3 days. He made an uneventful recovery and has remained well to date.

Comment

It should be noted that in Cases 1, 2, and 4 there was no previous history suggesting diverticulitis. Two of these patients presented themselves with lower midabdominal and right lower quadrant pain, rebound tenderness, and rigidity. The clinical picture in each suggested perforated appendicitis. In Case 3 the patient had a known stenosing lesion of the lower sigmoid by recent x-ray. The proctoscopic examination was an attempt to determine the exact nature of the lesion. Within 12 hours of the sigmoidoscopic examination in this patient symptoms of generalized peritonitis, substantiated by the presence of air under both leaves of the diaphragms, indicated perforation of a hollow viscus, and our natural assumption of free perforation of a diverticulum of the sigmoid proved to be correct. Upon examination of the pathology in this patient, we felt definitely that the moderate amount of air introduced ahead of the proctoscope contributed to the perforation. This may have occurred at a later time, because there was no attempt at walling off of the lesion by adhesions, but we have modified our policy of proctoscopic examinations in suspected diverticulitis in that a minimum of air will be introduced ahead of the sigmoidoscope during its introduction in these cases in the future.

In three of these four cases unusual trauma to the sigmoid colon preceded the acute free perforation. In Case 1 several vigorous enemata undoubtedly contributed to the perforation and avulsion of the sigmoid from the adherent bladder. In Case 2 the severe twisting strain to the abdomen preceding the onset of symptoms may have caused partial avulsion of the adherent sigmoid from the ileum. In Case 3 undoubtedly air introduced through the proctoscope contributed to the free perforation of a large and inflamed diverticulum.

In the past 10 years there has been a gradual metamorphosis in the surgical management of lesions of the colon encountered unexpectedly during the course of abdominal surgery. Prior to the advent of effective antibiotics to control the growth of Escherichia coli and other coliform organisms, primary resection of the colon without adequate preparation assured a high postoperative mortality rate owing solely to peritonitis. The intelligent use of such antibiotics as chlortetracycline (Aureomycin), oxytetracycline, and neomycin in the management of such cases has greatly reduced the incidence of peritonitis after colon surgery. Consequently surgeons, as exemplified by Judd,[5] and Guy and Werelius,[3] have become much more aggressive and direct in the treatment of colon lesions, in that primary resection with end-to-end anastomosis is now being employed in most lesions of the colon, whereas previously surgeons would have performed preliminary colostomies (Pemberton and associates[7]), exteriorizations, drainage procedures (Hughes and Shaw[4]), or other types of stage procedures.

In our practice we have encountered a number of lesions particularly in the cecum or ascending colon, such as carcinoma of the cecum, associated with acute appendicitis (2 cases), obstructing duodenal ulcer (one case), and chronic cholecystitis with cholelithiasis (one case). Lesions in other portions of the colon have been found unexpectedly, such as operable carcinoma of the stomach extending to the transverse colon (one case), perforated carcinoma of the rectosigmoid (one case), and extensive gangrenous colitis as a phase of ulcerative colitis requiring subtotal colectomy (one case). In none of these lesions were we permitted to prepare the colon in any way preoperatively, and yet we proceeded with a direct extirpation of the lesion without colostomy in each instance. Intravenously administered oxytetracycline was given

prophylactically every 12 hours for an average of 3 days during the postoperative period. All these patients, including the four in this series, recovered without incident, behaving in the postoperative period much like the carefully prepared patient. Open anastomoses were performed in all cases, care being taken to avoid any spillage. In Cases 1 and 2 and 4 in this series, owing to the extensive inflammatory induration of a segment of the sigmoid, it was elected to perform a primary resection of the involved segment of sigmoid. In Case 3 there was less involvement of the surrounding sigmoid, the pathology consisting merely of a large, very thin-walled diverticulum with surrounding peridiverticulitis and a perforation of the tip. Because of the presence of extensive diverticulosis throughout the remainder of the sigmoid and descending colon in Case 3 and the sharp localization of pathology, we simply resected the involved diverticulum, including its base, and closed the sigmoid without resecting an entire circumferential segment.

We have discontinued the preoperative preparation of elective colon surgical patients with oxytetracycline and chlortetracycline because of the high postoperative incidence of pseudomembranous ileocolitis. However, in patients where primary resection of colon lesions is necessary without any type of preoperative colon preparation, we have not hesitated to use prophylactic oxytetracycline intravenously in an attempt to prevent peritonitis. Other than mild temporary diarrhea in about one-half of the patients, we have noted no other complications from oxytetracycline used in this manner.

Summary

Four cases of acute perforation of a sigmoidal diverticulum, with generalized peritonitis as a rare complication of diverticulitis, are presented.

In two of the four cases presented typical symptoms and signs of perforated appendicitis with generalized peritonitis were exhibited.

The third case presented was presumably precipitated by a preliminary proctoscopy with increased air pressure in the sigmoid.

Definitive one-stage resections were performed in all cases with no postoperative morbidity or mortality.

The use of prophylactic intravenously administered oxytetracycline (Terramycin) postoperatively in unprepared cases undergoing colon surgery is discussed and advocated.

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Treatment of Inoperable Cancer by Intra-Arterial Administration of Mechlorethamine

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This report describes results obtained from the fractionated, regional intra-arterial administration of mechlorethamine hydrochloride (methyl-bis[β-chlorethyl]amine hydrochloride; HN_2) in a series of 60 patients with inoperable cancer. In each instance, oxytetracycline (Terramycin) was given concomitantly with the mechlorethamine. The effects of oxytetracycline were investigated in view of the observations of Barberio, who noted that the simultaneous administration of chlortetracycline (Aureomycin) and mechlorethamine seemed to have a greater adverse influence upon the cancer than mechlorethamine alone.

Methods and Procedure

The femoral artery is cannulated under direct vision, an incision being made inferior to Poupart's ligament, parallel to the course of the artery. After the artery has been mobilized, a small polyethylene catheter is inserted through it into the aorta. If the treatment is for cancer of the pelvis, the polyethylene tube is inserted a few inches above the bifurcation of the aorta. If efforts are being made to alleviate hepatic or gastric cancer, the catheter is threaded into the aorta to the level of the celiac axis. It is then sutured to the femoral artery with absorbable surgical (gut) sutures. A needle and two-way stopcock inserted into the exposed end of the catheter permit administration of the medication.

The following regimen has been adopted. Tourniquets are placed around each thigh. Mechlorethamine hydrochloride, 10 mg. dissolved in 10 ml. of isotonic saline, is injected daily. This is followed by the administration of 0.5 to 1 gm. of oxytetracycline dissolved in 100 ml. of isotonic saline. Oxytetracycline given intra-arterially is irritating, and the patients often complained of "electric shock-like sensations" extending up and down their bodies and into their legs. The greater the concentration of the oxytetracycline, the more severe the symptoms. Inasmuch as oxytetracycline is in the acid range, with a pH of about 4, it is not surprising that these symptoms are produced. These untoward effects are minimized by a greater dilution of the oxytetracycline, slower administration, and dissolving the drug in an 0.1% solution of procaine. If the patient had any significant symptoms at the completion of the injection, 3 cc. of 0.1% procaine was injected through the intra-arterial catheter, which served to relieve the spasm produced by the oxytetracycline.

This treatment was given usually for five days, with an average total dose of 50 mg. of mechlorethamine hydrochloride and 3 to 5 gm. of oxytetracycline. Efforts to increase this dosage, in our experience, did not benefit the patient. Moreover, it aggravated the untoward effects inherent in this therapeutic regimen.

The intra-arterial mechlorethamine and oxytetracycline was given to patients bearing the following tumors: 5 patients with lymphomas—1 reticulum-cell sarcoma, 3 lymphosarcomas, and 1 Hodgkin's disease; 23 patients with cancer of the rectum and colon; 5 patients with cancer of the uterus—2 cancers of the cervix, 1 endometrial adenocarcinoma, 2 leiomyosarcomas of the uterus; 14 patients with cancer of the ovary; 3 patients with cancer of the stomach; 2 patients with diffuse metastases, primary site of tumor not known; 1 patient with cancer of the prostate; 1 patient with extensive carcinoma of the head and neck (this patient treated by intra-carotid catheterization); 1 patient with diffuse melanoma; 1 patient with hepatoma; 1 patient with cancer of the pancreas; 3 patients with disseminated metastases from primary breast cancer.

Results

The results will be described according to type of tumor treated.

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From the Pack Medical Group.

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1. *Lymphoma.*—As would be expected, the most marked results were obtained in patients with various lymphomas. The five patients treated enjoyed some palliation. The one exception had a retroperitoneal lymphosarcoma that had infiltrated the spine and produced extensive pain in the lumbosacral region and both lower extremities; he died two months later from widespread disease. Two others, who also died, enjoyed palliation which lasted from nine months to four years. One patient with extensive Hodgkin's disease, almost completely filling the abdomen, manifested a marked shrinkage of the abdominal mass after administration of mechlorethamine intra-arterially.

CASE 1.—*Abdominal Hodgkin's Disease*

A 48-year-old man was hospitalized on July 11, 1952. He had been explored by his local physician previously because of symptoms and signs of intestinal obstruction. A huge mass was observed which filled the entire left half of the abdomen, extended to the midline impinging upon the aorta, and filled the pelvis. The patient developed a spontaneous colostomy shortly after the operation, which drained a constant stream of semisolid fecal material. A biopsy revealed Hodgkin's disease.

From July 15 to July 21, 1952, inclusive, he received six intra-arterial injections of mechlorethamine, totaling 60 mg., and 6 gm. of oxytetracycline. He suffered severe pain during the therapy, and the persistent drainage from the colostomy was bothersome. Shortly after completion of the treatment, colostomy excretions ceased and the colostomy closed spontaneously. The mass decreased until it could not be palpated, and the abdomen appeared normal in every respect. The patient was given postchemotherapy irradiation. With a million-volt generator, x-ray therapy was given via a large port (23×23 cm.) over the anterior abdomen and a similar-sized port over the posterior abdomen with the following factors: 3 ma., 70 cm. target-skin distance; he received 300 r×10 to each of two portals. He tolerated this therapy well and remained asymptomatic for two years, when he developed evidence of involvement of the chest and cervical region which responded well to sporadic medium-volt x-ray therapy. He died five years later from recurrent abdominal Hodgkin's disease.

Comment: It is difficult to evaluate the exact role of this form of administration of mechlorethamine to patients with lymphomas because this group of neoplasms will respond to almost every form of chemotherapeutic or radiotherapeutic agent. However, in patients with extensive abdominal disease, it was a distinct impression that the intra-arterial route of administration offered an improved method of administering the medicament and afforded an increased concentration of the chemotherapeutic agent to the tumor within the abdominal cavity.

Cancer of the Ovaries.—Of the 14 patients bearing cancer of the ovaries treated by intra-arterial mechlorethamine, none is alive; all had extensive disease and were treated in this manner as a last resort. The average duration of life from completion of the treatment with mechlorethamine was 6 months and varied from 1 to 18 months. In half of the patients there was relief of pain. In almost half there was a shrinkage of the mass. In two patients who had suffered intestinal obstruction, there was a lessening of the obstruction. The course of Case 2 is presented in abstracted form to reveal the relief from obstruction of the intestine and of the right ureter following this regimen.

CASE 2.—*Carcinoma of the Ovary Producing Frozen Pelvis*

The patient had a hysterectomy performed in 1946. The pathology report revealed fibromyomas of the uterus, adenomyosis interna, one ovary with multiple follicular cysts, and endometriosis in tissue from the pouch of Douglas. Cancer was not found. In May, 1951, she developed severe abdominal pain. Her physician found a frozen pelvis and an enlarged lymph node in the left supraclavicular region which proved to contain metastatic ovarian cancer. A course of deep x-ray therapy administered to the lower abdomen failed to affect the growth of the tumor significantly.

On examination here, on April 8, 1952, the entire pelvis appeared infiltrated by tumor which obstructed the right ureter so that the kidney failed to excrete radiopaque material and compressed the left ureter also. The BUN was within normal limits. She also had clinical and radiologic evidence of intestinal obstruction at the level of the rectosigmoid junction. Because of the extensive pelvic cancer, with intestinal and ureteral obstruction, the patient was hospitalized on April 28, 1952. She was given a course of 50 mg. of mechlorethamine hydrochloride plus 5 gm. of oxytetracycline in five days through the left femoral artery. During the course of therapy the BUN increased to 90 mg. per 100 cc., but it returned to

Fig. 1A.—Intravenous pyelogram illustrating nonfunctioning of the right kidney due to pressure from a massive ovarian cancer. The patient also had rectal abduction.

Fig. 1B.—Intravenous pyelogram taken after a course of intra-arterial mechlorethamine, demonstrating a functional right kidney.

normal levels after the oxytetracycline was discontinued.

The patient was relieved of her symptoms. All symptoms and signs of intestinal obstruction subsided, with softening and shrinkage of the pelvic mass. An intravenous pyelogram revealed both ureters functioning (Figs. 1A and 1B). The benefit, however, was short-lived; in August, 1952, she developed gastric obstruction from tumor in the upper abdomen, and she died several weeks later.

Uterine Cancer.—The two patients with carcinoma of the cervix and one with carcinoma of the endometrium had only slight relief of symptoms. Two patients with leiomyosarcoma enjoyed relief from a softening of the masses and diminution of the formation of ascites. In one, the duration of benefit was short-lived, as she survived only six months after treatment; the second patient, with diffuse hepatic metastases from a uterine leiomyosarcoma, enjoyed significant palliation for one and one-half years, after which she died.

CASE 3.—*Metastatic Leiomyosarcoma to the Liver, Primary in the Uterus*

A 60-year-old white woman had suffered "stomach difficulties" for 14 months. An exploratory laparotomy revealed a large tumor mass in the pelvis with metastases to the liver. Radiation therapy failed to reduce the size of the tumor significantly.

When first seen by us, the patient complained of a pressure sensation in the epigastrium. There was a large, discrete, and globular tumor mass with smooth edges involving the left upper quadrant and extending 12 cm. below the costal margin. It was not freely movable but did move on respiration. The patient had lost weight, was nauseated, and had postprandial vomiting.

At laparotomy, on Jan. 11, 1955, a large tumor was observed which almost completely replaced the left hepatic lobe, and a number of discrete nodules varying from 1 to 3 cm. in diameter were found scattered throughout the right lobe. Since the tumor was obviously inoperable, intra-arterial mechlorethamine, consisting of 50 mg. mechlorethamine hydrochloride and 5 gm. oxytetracycline, was administered fractionally at the level of the celiac axis. Eight months after the chemotherapeutic regimen the mass was softer and the patient was asymptomatic. She had gained 8 lb. (3.6 kg.). The hemoglobin at that time was 12 gm. (80%), with a red blood cell count of 3,820,000; the white blood cell count was 6550, with a normal differential count. A liver profile at the same time revealed the phosphorus to be 3.8 mg. per 100 cc., alkaline phosphatase 8.2 S. J. R. units, bil-

irubin 0.5 mg. per 100 cc., cephalin flocculation negative, thymol turbidity less than 5, total protein 7.8 gm. per 100 cc. She suffered a recurrence of symptoms due to regrowth of the liver mass and died 18 months after the intra-arterial chemotherapy.

Gastric Cancer.—Of three patients bearing gastric cancer, none had relief; in fact, one developed intractable vomiting which persisted until death. The clinical impression is that this form of therapy is not indicated for hopeless gastric cancer, since the symptoms were not relieved satisfactorily and the average duration of life after the completion of treatment was only three months.

Colon and Rectal Cancer.—Of 23 patients suffering from this form of cancer, all died from 1 to 36 months after therapy, the average being 5 months. However, perineal pain, so characteristic of infiltrating rectal cancer, which occurred in 75% of the patients treated, was usually relieved, sometimes dramatically. Unfortunately, this relief was short-lived. There was some shrinkage of the mass in one-fourth of the patients, and one-fourth obtained no relief whatsoever. In one patient with intestinal obstruction, some relenting of the obstruction obtained. Another enjoyed relief from paralysis subsequent to cord involvement from rectal cancer (Case 4).

CASE 4.—*Rectal Cancer Infiltrating the Spine*

The patient was subjected to an anterior resection of the sigmoid colon and an end-to-end anastomosis for cancer of the sigmoid in November, 1951. After remaining asymptomatic for nine months, he developed a gradually increasing paralysis of the lower extremities with inability to control bowel and bladder function, obviously the result of tumor infiltration of the spinal cord. Roentgen examination at the Presbyterian Hospital, New York, revealed only osteoarthritis. Other studies, including intravenous pyelography, revealed no evident disease. The patient was subjected to a course of deep x-ray therapy at Presbyterian Hospital, New York, with no benefit.

When observed by us, the patient had complete paralysis of the lower extremities, bowel, and bladder. He was given a course of intra-arterial mechlorethamine hydrochloride (50 mg.) and oxytetracycline (5 gm.) in December, 1952. The paralysis of the extremities receded, enabling him to walk. Except for recurrent infection of the urinary tract associated with an indwelling catheter (he never regained urinary continuence), the patient remained asymptomatic for two and one-half years and died as a result of metastases to the liver.

Comment: Because of prolonged suffering of patients with inoperable rectal cancer, this form of therapy would seem indicated, especially for the control of the severe perineal and lumbar pain. Although the therapy could not be said to produce increased longevity, it did produce symptomatic improvement.

Miscellaneous Cancers.—Two patients with diffuse metastases from unknown primaries showed transient shrinkage of the tumors and a sense of well-being for an average duration of six months. One patient, with extensive carcinoma of the oral cavity, died the day after the second dose of mechlorethamine was introduced into the common carotid artery. There occurred in one patient with diffuse melanoma a shrinkage of a huge metastatic deposit within the liver, but he died four months later as a result of a cerebrovascular accident. Two patients with primary hepatomas treated by this regimen enjoyed a slight temporary sense of well-being but died four and nine months, respectively, after therapy. One patient with a cancer of the pancreas received no benefit, and three patients with diffuse metastases from primary breast cancers had doubtful improvement.

Complications

Complications of this form of therapy can be divided into generalized and local effects.

The most persistent and common complication was a depression of the hemopoietic system. All patients developed not only leukopenia but anemia, which required transfusions for control. Bone marrow studies revealed the anticipated depression of all cell types. A rather unusual finding was the selectivity of the effect on the blood cells. In all patients there was a reduction of eosinophils. The reduction of red cells or white cells varied from patient

to patient. In some, a severe anemia, without a marked leukopenia, occurred, whereas others developed a severe leukopenia, the white cell count dropping to 500 to 700 per cu. mm., with the red cell mass but slightly affected. Some developed depression of all cellular elements. In addition, the various members of the leukocyte series were selectively affected. Thus, in certain patients a severe lymphopenia occurred, with but slight decrease in the neutrophils, while in others the converse occurred, with a severe neutropenia and a relatively slight depression of the lymphocytes. The explanation for these responses is enigmatic. Whether they represent some manifestation of the damage to the hemopoietic system by the tumor or some sort of selective response to the therapeutic agent cannot be stated. All patients revealed toxic granulations within the polymorphonuclear leukocytes; all had platelet depression, but in only 2% was this depression severe enough to produce bleeding tendencies. The magnitude of the hemopoietic depression was generally proportional to the degree of metabolic impoverishment of the patient and the amount of previous irradiation received. Despite the severe leukopenia which occurred in some patients, no generalized infections were observed. It is believed that the administration of oxytetracycline concomitantly with mechlorethamine permits the administration of rather large doses of mechlorethamine without fear of overwhelming infection even with the depression of the leukocytes.

Nausea and Vomiting.—Nausea and vomiting occurred in most of the patients, although these symptoms were less evident than when the mechlorethamine was administered intravenously. However, some were entirely free of this complication. All patients with gastric cancer treated by this agent suffered severe nausea and vomiting. In one it was intractable even in the absence of obstruction. Conversely, four pa-

Fig. 2A.—Purpuric spotting of leg after a course of 50 mg. mechlorethamine hydrochloride and 5 gm. oxytetracycline.

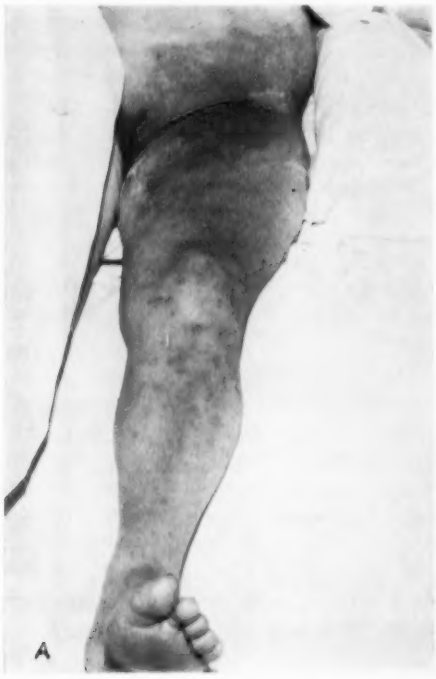

Fig. 2B.—Close-up view of the same patient, illustrating a brawny induration of the region where the mechlorethamine was injected.

Fig. 3.—Anterior and posterior views demonstrating superficial patchy gangrene of the lower extremity after the administration of 50 mg. mechlorethamine hydrochloride and 5 gm. oxytetracycline in five days. The extremity healed spontaneously in 21 days.

tients with intestinal obstruction who had suffered severely before therapy enjoyed palliation of these symptoms as the obstructing tumor decreased in size. Gastrointestinal atony and adynamic ileus developed and produced abdominal distention, sometimes to a severe degree. This was relieved in each instance by bethanechol (Urecholine) chloride in rather large doses. This response probably represents a parasympathicomimetic result of the therapeutic agent.

Various local changes occurred in the tissues receiving the drugs. Brawny induration sometimes in and sometimes proximal to the site of the injection occurred. In two patients hematomas developed following the withdrawal of the catheters. These became infected and required laborious therapy for their control.

Patchy Gangrene.—Four patients developed patchy superficial areas of necrosis involving the extremity in which the mechlorethamine and oxytetracycline were administered. The lesions varied from discrete small areas 1 to 3 cm. in diameter scattered over the thigh and lower leg to larger, confluent regions. In no patient was this observed when mechlorethamine was administered alone, and it is believed that these lesions are the result of spasm induced by the administration of the oxytetracycline.

Increased Blood Urea Nitrogen.—All patients who received large doses of oxytetracycline developed an increased blood urea

nitrogen. If normal at the commencement of this regimen, the blood levels dropped to normal values soon after the cessation of the oxytetracycline administration. Kidney function remained normal. This increased BUN is due to the oxytetracycline, which either competes with the urea for excretion by the kidney or causes the production of increased quantities of urea.

It is of interest in this respect that Klopp et al. have demonstrated hyperbilirubinemia in patients who receive large doses of chlortetracycline. No effect on the blood urea nitrogen occurred. No liver damage was observed. Accordingly, chlortetracycline may be substituted for oxytetracycline in a patient who has developed a high blood urea nitrogen on the mechlorethamine-oxytetracycline regimen.

Comment

The intra-arterial administration of mechlorethamine offers a means of administering a chemotherapeutic agent directly to the organs bearing the tumor. The results of these studies would show that in selected cases a therapeutic benefit accrues and that the intra-arterial method of administering mechlorethamine is more efficacious than the intravenous technique. Sometimes the results are dramatic—for example, causing intestinal obstruction to relent. Patients who are acutely ill and those who are metabolically impoverished will not respond. The severe bone marrow depression resulting from this form of therapy necessitates a critical evaluation of the patient's hemopoietic system. If this is severely damaged, this form of therapy is contraindicated. In the majority of patients who suffered a hemopoietic depression from this treatment, there was a prompt improvement following cessation of therapy.

Lymphomas responded best to this form of treatment. At times disappearance of large masses was observed. Surprisingly, patients with cancer of the rectum and colon who suffered severe perineal pain enjoyed relief from this troublesome symptom. The response of the other types of cancer varied.

The concomitant administration of oxytetracycline appeared to produce a synergistic effect, with a better response than when mechlorethamine was the sole therapeutic agent. It is impossible to state with any degree of definiteness whether this is so; it is merely a clinical impression. The antibiotic provides a satisfactory procedure for protecting against infection. When given intra-arterially, it must be well diluted. In our latter cases it was administered as a 0.5% solution, the administration being made with an arterial pump.

A constant observation was the transient effect of the chemotherapeutic regimen. Each patient who enjoyed relief of symptoms did so for a short period. There seemed to be an escape from the benefits conferred by the mechlorethamine, and the cancer then appeared to grow again as before the chemotherapeutic regimen. Because of this, a course of deep x-ray therapy is given those patients who can tolerate it following the course of mechlorethamine. Although various authors describe the results of treatment with mechlorethamine as similar to those of x-ray therapy, Shreck has shown that these agents exert different cytotoxic effects, and advantage can thus be taken of two forms of mechanisms destructive to the cancer cells.

In this series it was necessary to hospitalize each patient to subject him to the operative procedure for the insertion of the catheter. Some of the patients required special nurses; all required transfusions.

Accordingly, the decision to administer mechlorethamine to patients by the intra-arterial route by the techniques described must encompass all factors, which include the type of cancer, extent of cancer, metabolic status of the patient, and the realization that the beneficial effects are, at best, transient. It should not be routinely used for all patients with cancer in whom other forms of treatment have been exhausted. We have discontinued the use of intra-arterial oxytetracycline because the discom-

fort and complications are greater than its benefits.

Summary and Conclusions

The intra-arterial route of administering mechlorethamine offers a method of obtaining a high concentration of the drug in the tumor.

The concomitant administration of oxytetracycline in large doses augments the effect of the mechlorethamine and prevents infection despite severe leukopenia. Its administration into the artery produces arterial spasm and patchy gangrene in some patients; hence its use is not advocated.

Of 60 patients treated by the intra-arterial administration of mechlorethamine and oxytetracycline, most have enjoyed some palliation but only a questionable increased longevity.

The palliation is always transient. Accordingly, a postchemotherapeutic course of deep x-ray therapy is given if the patient has not already received radiation therapy.

Lymphomas respond best to this form of therapy. Relief of perineal pain was experienced by patients with rectal or colonic cancer.

Patients with gastric cancer or breast cancer did not respond favorably.

The treatment produces hemopoietic depression and at times other complications. Its use should be employed only after critical evaluation of the patient's metabolic status.

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Segmental Liver Revascularization

An Experimental Study

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The experimental methods of increasing the vascularity of the liver focus on two types of procedure: (1) creation of perihepatic adhesions [1]; and (2) arterialization of the portal vein stump after performing an end-to-side portocaval shunt.[2] Vineberg's observation [3] that implantation of the internal mammary artery into the myocardium will result in collateral circulation has not been experimentally applied to other organs.[4,5] The present study was undertaken for investigative purposes in the hope that it might lead to a method of segmental arterialization of the liver in which both a revascularized lobe and control lobes could be evaluated in the same animal.

Method

Ten, large, healthy, greyhound dogs were anesthetized with pentobarbital (27 mg. per kg.). The peritoneal cavity was explored in each instance through a high midline incision under aseptic precautions. A splenectomy was then performed. The splenic artery, or a very large branch of it, was stripped of perivascular fat and accompanying veins. Bleeding from the vessel was controlled with a bulldog clamp.

Prior to implantation of the splenic artery into a convenient lobe of the dog's liver, a 1 in. tunnel was prepared with a blunt, small, curved hemostat. The cut end of the splenic artery was then embedded into the prepared tract by the use of a fine silk traction suture and a large, curved, round needle (Fig. 1). Maintenance of the implanted vessel was assured by fixation of the silk traction suture over a small, rubber tube on the surface of the liver. Upon release of the bulldog clamp, pressure with gauze was applied to the liver edge for five to ten minutes for hemostasis. The abdomen was then closed in layers and the dogs were observed for varying periods of time. Iodopyracet (Diodrast) and methylene blue injection studies and direct dissections were carried out to determine the patency of the arterial implants. Iodopyracet studies were performed after liver lobectomy to obtain accurate detail of the vascular patterns on film in cardboard casettes.

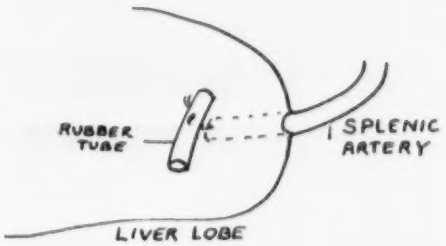

Fig. 1.—Technique of embedding and securing artery in a liver lobe.

Results

All animals survived the operation and the period of observation afterward. At the time of killing (one to six months), there were significant and dense omental adhesions about the site of the arterial implantation. In each instance the splenic artery was shown to be patent with functioning collaterals after two months of implantation by the radiographic injection technique. Persistence of this collateral flow was again demonstrated in the animals killed after three to six months of observation (Fig. 2) by methylene blue and iodopyracet study. The considerable resistance to injection of the splenic artery always suggested obstruction until the x-ray films were developed or the dye was visualized in the hilar hepatic artery of the severed lobe. In all but one study the collateral circulation appeared to be between the splenic artery and the hepatic

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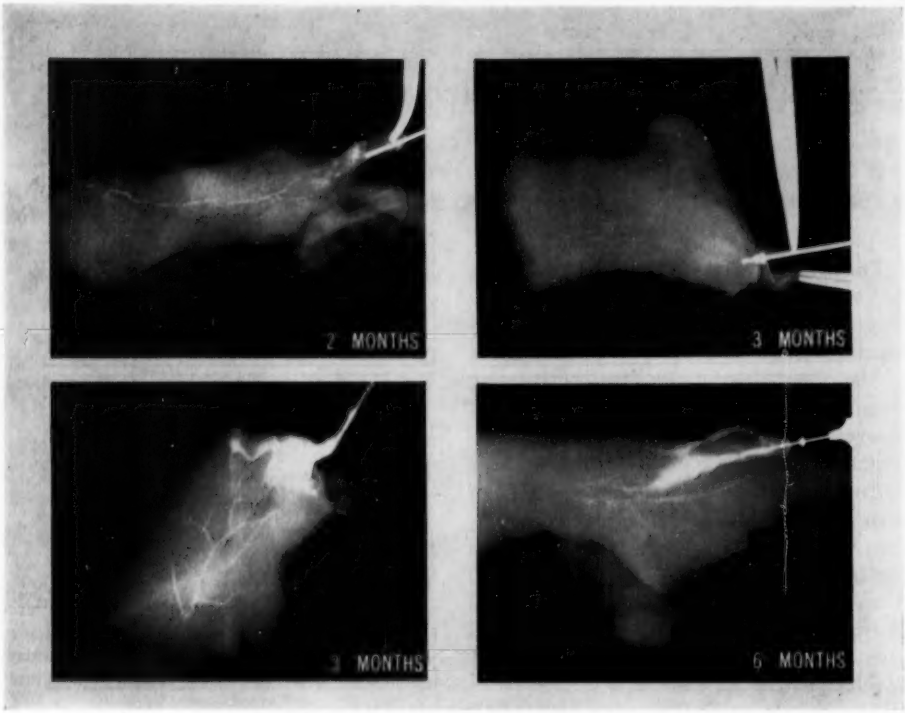

Fig. 2.—Iodopyracet injection studies of the liver lobe through the stump of the implanted splenic artery. Extreme resistance to injection suggested total blockage in each instance until the films were developed and collaterals were evident.

lobular arteries. An arteriovenous communication was suspected in one animal; however, a false passage of the contrast medium injection needle may have occurred.

Comment

The observations of Vineberg and colleagues,[6] Glenn and Beal,[7] Neptune,[8] and Bigelow[9] demonstrated that some circulation in the myocardium can result from direct implantation of an adequate systemic artery. Tissue anoxia and different arterial pressures in the host tissue and the implanted artery appear to influence the success of collateral communications. Vineberg showed a 76% successful anastomosis rate when the internal mammary artery was implanted into ischemic heart muscle, but his successful implant rate dropped to 46% when employing normal myocardium in the experimental animal. Experience and different techniques further influenced the diversity of results.

In the current liver studies, recanalization of the splenic artery and patency of collateral channels were demonstrated in each instance where the animal was killed after eight weeks. Undoubtedly, functioning vessels communicated much sooner; however, it was not possible to satisfactorily demonstrate them by radiographic technique at four weeks in this series. Whether new vessels grow outward from the severed end of the splenic artery or whether they invade the potential clot from the raw surfaces of the traumatized liver tunnel was not determined. Possibly a combination of these sources of endothelium was involved.

The negligible intrahepatic hematoma formation would appear to be related to

the physical tissue resistance of the liver against the leaking splenic artery. Serious hemorrhage from the liver tunnel was never a problem. Immediate excessive bleeding was a sign that the implanted vessel had pulled loose, making it necessary to reposition the artery. In each instance bleeding was controlled effectively by gauze pressure for five minutes on the liver adjacent to the site of arterial implantation.

Inasmuch as normal, healthy dogs were studied, it is difficult to speculate on directional flow and differential arterial pressures in the liver and in the splenic artery. Evidence of strong arterial bleeding from the proximal end of the severed splenic artery at the time of killing suggests arterial flow toward the liver.

The exact mechanism of recanalization is not clear; proteolytic enzyme action, phagocytosis, and vascular pressures must play a role. The well-organized clot, observed at the distal end of the splenic artery, would result in initial stagnation of the splenic artery flow. The splenic artery pressure would dominate on the proximal side of the recanalized clot while small capillary and hepatic arteriolar pressures would be found on the distal side of the implant. With time, the new connecting vascular channels enlarge and an equilibrium would be anticipated between the hepatic artery and the splenic artery pressures. Just why the collaterals usually seem to communicate with the hepatic arterial circulation in a selective fashion rather than to form arteriovenous fistulae is also not clear.

In the normal dog liver, implantation of the splenic artery resulted in no hypertrophy or gross abnormality of the affected liver lobe. Microscopic examination showed no cellular architectural differences between the revascularized and normal liver lobes, except for the plexus of new vessels which formed at the site of implantation. Collateral flow studies are currently in progress on dogs in whom the splenic artery has been implanted into the left kidney.

Summary and Conclusions

Direct implantation of the splenic artery into a normal canine liver lobe can result in endothelial proliferation and collateral circulation with hepatic vessels. From a quantitative standpoint the amount of collateral anastomoses created by this technique in normal liver tissue is not impressive.

Mr. Clyde Evers, Mr. Albert Johnson, Mrs. E. Domutz, and Miss E. Paulak gave technical assistance.

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Primary Acute Mesenteric Lymphadenitis

A Review of One Hundred Ninety-Eight Cases

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The paucity of literature and textbook references on acute mesenteric lymphadenitis has been an incentive to me to review all cases of the disease which had been hospitalized in the Albany Hospital during the years from January, 1940, to August, 1956, inclusive. One hundred ninety-eight cases were analyzed. Every surgeon has operated upon cases which apparently gave a sign-symptom complex of acute appendicitis, and yet there was found at operation a normal appendix but with enlargement of the mesenteric lymph nodes, most especially those nodes distributed about the terminal ileum and the appendicocecal junction. The patient recovers, and recovery is attributed to the appendectomy. Can one evaluate these cases to such a degree that in many cases surgical procedures are unnecessary? And is one able to define a sign-symptom complex which might very well encompass the diagnosis of primary acute mesenteric adenitis? Or are the symptoms and signs so bizarre as to necessitate "the taking of no chances" and operate?

With these questions in mind, the review was made. Inflammation of the mesenteric lymph nodes was recognized and discussed as early as the 18th century. The diagnosis was usually made after the patient came to autopsy (Adams [1])! Within the past few decades the affection has been more seriously considered, and there are those who consider the disease to be a definite clinical entity with signs and symptoms so pronounced as to form a diagnosis and not attended with dogma. It is a disease of everyday occurrence. It is one of the common causes of acute abdominal pain in children, and, as Asencio [2] remarked, "It is an occasional puzzling affection of adults." Despite the fact that Weeder [19] makes the statement that "the differential diagnosis between mesenteric lymphadenitis and acute appendicitis is academic," I can envision the statement as being somewhat too broad in its application.

The etiology of acute mesenteric lymphadenitis has given rise to varied theories, but at the present all of them are based, more of less, on hypothesis.

The seasonal incidence has been supported by Rosenburg.[14] From the review of our cases there is nothing to indicate that there is any relationship whatsoever. The supposition has been expounded that during certain months in the year upper respiratory tract infections have been the probable cause for the appearance of acute mesenteric adenitis. This is not borne out by our statistics (Table 1 and Fig. 1).

Weeder brings up the possibility that the enlarged nodes are due to some allergic reaction in the absorption of a histamine with a possible bacterial sensitivity of the gastrointestinal tract. This is based on hypothesis and has never been substantiated by many investigators.

Veiled enteritis has been hypothesized.

Despite the fact that Goldberg [10] has isolated a hemolytic Streptococcus in the throats of 16 patients with mesenteric adenitis, the sterility of the nodes does not, in my opinion, substantiate this assumption, though one must agree that foci of infection are probably important etiologic factors. FitzGerald,[8] who has been most interested in the laboratory and clinical investigation of this disease, is adamant in his statement

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TABLE I.—*Number of Cases in Which Acute Mesenteric Lymphadenitis Appeared by Years and Months During 1940 to 1956*

Seasonal
1940 (2); 1941 (5); 1942 (3); 1943 (4); 1944 (5); 1945 (12); 1946 (4); 1947 (7); 1948 (19); 1949 (13); 1950 (15); 1951 (20); 1952 (20); 1953 (21); 1954 (27); 1955 (13); 1956 to August (8).
Total—198
Months
January (15); February (19); March (18); April (14); May (17); June (26); July (9); August (14); September (17); October (15); November (21); December (18).
Total—198

that "infection with the streptococci is of no importance in the causation of this disease." Indeed, from a bacteriologic standpoint all cultural tests, with very few exceptions, have proved negative. Weeder, Christopher,[6] FitzGerald, and others support this assertion.

Webster [18] found pinworms in the appendix in 7% of patients suffering from mesenteric adenitis. In our series five cases presented their occurrence. I cannot help but feel that the finding of Oxyuris vermicularis was coincidental and should not be considered on an etiologic basis.

Serious consideration should be placed upon the relation between upper respiratory infection and acute mesenteric lymphadenitis in that so frequently mesenteric adenitis follows in the wake of respiratory infections. Whether this is coincidental or whether it is an etiologic factor is still open to debate. All investigators, including physicians and surgeons, are of the opinion that this relationship should always be borne in mind. Gross [11] emphasizes the fact that "almost invariably the affection accompanies a respiratory infection, so that examination of the pharynx, nose, and chest is most important." FitzGerald states that "upper respiratory tract infection is a significant predisposing factor" and that 56% of his 109 cases gave a history of upper respiratory infection within one month of the present illness. Freeman cited Heilman, who, while working in the Rosenow laboratory, cultured organisms from the throats of patients found to have mesenteric adenitis at operation and inoculated rabbits with these organisms. Enlarged lymph nodes of the mesentery of the small intestine developed in 72 hours. This investigator suggested, therefore, that the disease could be transmitted from one person to another through the nasopharyngeal secretions. He further stated, in support of this evidence, that there is the more than frequent history of recurring attacks of upper respiratory infection in these patients preceding their attacks of abdominal pain. Adams speculated that it is not unlikely that enlarged mesenteric lymph nodes are a local manifestation of a generalized condition, having its origin in an upper respiratory tract infection.

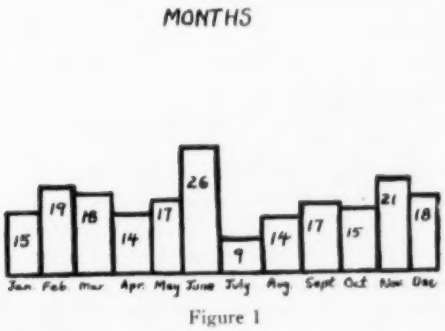


Figure 1

In our series there was an incidence of 33.8% (Table 2).

The appendix and small intestine have received the major consideration as etiologic factors, and yet here too there has been a great deal of speculation. From an anatomic viewpoint one must recognize the fact that the appendiceal lymphatics drain into the ileocecal chain and that in the vast majority of cases the enlarged nodes are in close proximity to the appendix, the

TABLE 2.—*Signs and Symptoms of Acute Mesenteric Lymphadenitis in 198 Cases*

Sex	
Males	106
Females	92
Previous attacks	109
Respiratory	67
Nausea and vomiting	70
Malaise	52
Anorexia	45
Adenopathy	55
Rigidity (true splinting)	18
Guarding or voluntary	20
No rigidity or guarding	32
No mention of rigidity or guarding	108

ileocecal junction, and the terminal ileum. On the other hand, as pointed out by Asencio, the most virulent appendicitis need not produce reactive mesenteric adenitis. The stimulation of a large portion of the lymphoid tissue in the submucous coat of the appendix has brought forth the theory that hyperplasia of this tissue may block the lumen of the blood supply (Christopher).

On the basis of investigation Wangensteen[17] emphatically stated, "We cannot easily abandon the notion that obstruction is an important item in originating the disease and that the presence of a mechanism inhibiting to the outflow, from the lumen of the appendix interferes with the satisfactory evacuation of its contents." From the histologic reports in our series, 31 patients showed lymphoid hyperplasia with partial or complete obliteration of the lumen. These findings indicate that lymphoid hyperplasia with partial or complete obliteration of the lumen may be a possible etiologic factor (Table 3).

Many are of the opinion that an appendectomy is followed by a cure in the high percentage of cases and support the view that the appendix is the offending agent; but one should, on the other hand, recognize the fact that acute mesenteric lymphadenitis is, on the whole, a self-limited disease and that the patient might very well have recovered despite operation. Another point must be brought into consideration, and that is that a great many cases have not been followed up, and one does not know whether there will be recurrences.

I do not agree with Asencio and others that when mesenteric adenitis is observed in the operating room a reactive adenopathy involving the lymphatics of the whole mesenteric system is involved. This may be true in certain instances but is not generally found at operation.

An inspection of Table 3 shows the histologic findings of the appendices removed at operation.

Is it possible to make a satisfactory diagnosis of primary acute mesenteric lymphadenitis, thereby avoiding surgical intervention for the removal of the appendix? The answer to this question is one that requires a good deal of analysis before answering in either the affirmative or the negative.

Every experienced surgeon has operated upon patients, especially children, who presented a history and physical signs more or less typical of appendicitis. Upon operating, it was found that the appendix was apparently negative and that acute mesenteric adenitis was present (Table 3).

In order to make even a tentative diagnosis of this condition, many factors have to be brought into consideration. One of the most important of these is the past history of the patient. The history of previous attacks similar to the present one is noted in a vast majority of cases (Table 2). In our series 55% gave such a history. The duration must be considered as a factor.

TABLE 3.—*Histologic Findings Following Appendectomies and Other Operations*

Operations	
Appendectomy	121
Exploration	1
Excision mesenteric lymph nodes	2
Total	124
Histology	
Healed appendicitis	39
Negative appendix	27
Healed appendicitis with lymphoid hyperplasia	26
Healed appendicitis with oxyuriasis	5
Of 121 appendectomies	
Early acute appendicitis	8
Subacute appendicitis	4
Chronic appendicitis	3
Chronic appendicitis with obliteration of lumen	4
Fibroid appendicitis with partial obliteration of lumen	5
No Operations	74
Mortality—1—cardiac arrest	

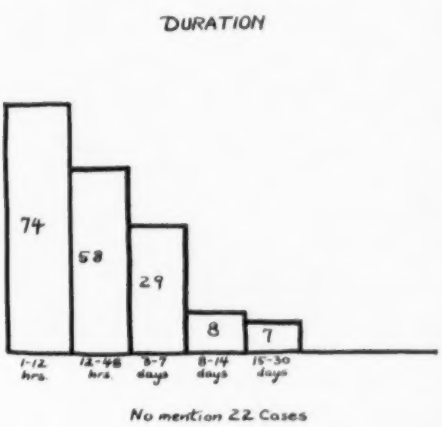


Figure 2

All are in agreement that the duration of the period from last attack to present condition may vary from a few hours to many days. In this series the duration was as follows: 1-12 hours, 74 cases; 12-48 hours, 58 cases; 3-7 days, 29 cases; 8-14 days, 8 cases, and 15-30 days, 7 cases (Fig. 2).

Acute mesenteric adenitis is essentially an affection of children and young people, though a patient may be affected at any age (Fig. 3). The affection is supposed to predominate among males. This is confirmed in our series, in which there were 106 males and 92 females (Table 2).

The clinical signs and symptoms are quite bizarre, and there is variance in the opinions of those who have been especially interested in the affection. Gross, in characterizing the disease, states that "nausea and vomiting seldom accompany this condition," while FitzGerald, who has recently written on the subject, finds that "vomiting is common" and Young refers to "when the abdominal symptoms of pain, nausea and vomiting do develop." Christopher, in giving the clinical symptoms, does not include vomiting as an accompanying symptom. Thus, there is a divergence of opinion. In our series nausea and vomiting were present in 35.3% of the cases (Table 2).

Malaise and anorexia were observed in 49.4% of the cases in this series. Dizziness and headaches were noted in a few cases. These were not prominent symptoms (Table 2).

When one considers the affection as being a generalized disease of the lymph nodes, one is prone to consider as pathognomonic, or at least suggestive, the finding of adenopathies in these patients, as they have an important bearing on the above hypothetical etiologic factor. In this series 28% presented either general or regional adenopathies. It was interesting to note, however, that in none of these cases were there any clinical evidences of an acute inflammatory disease, or was there any indication but that they were normal hypertrophic and hyperplastic, as has been so often found. Moorman's [13] observation on the incidence of palpable lymph nodes is interesting in that he found "lymph nodes, from 1 to 2 cm. in diameter, in a large percentage of healthy males" and that, in the absence of other findings, these nodes have no significance when discrete, nontender, and freely movable.

A difference of opinion is found between the existence of true rigidity, in which definite splinting is present, and the so-called guarding, or voluntary rigidity. Gross lays very little stress on the occurrence of true rigidity, while Christopher denies the existence of muscular spasm. Young emphasizes the opinion that "moderate rigidity" does exist. In the experience of those at the Albany Hospital and as a result of my own observation, there are cases in which

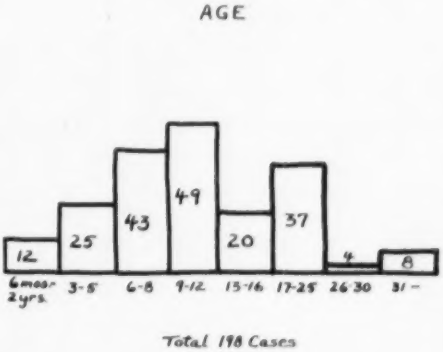
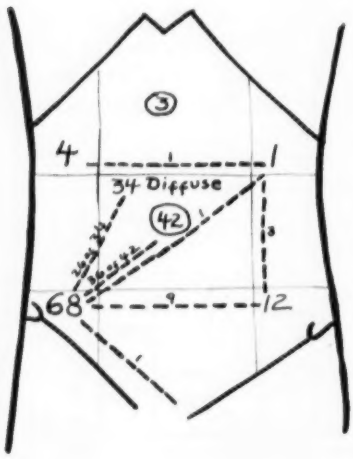


Figure 3

true rigidity is present; however, these cases are few and far between and in our series may be summarized as follows: True rigidity or definite splinting was found in only 18 cases, while voluntary rigidity, or guarding, was noted in 20. Many of the cases have no record as to the existence or nonexistence of this sign, but about 32 have been registered as "no rigidity" (Table 2).

Pain and tenderness is present in nearly 100% of the cases; of course, there are exceptional ones in which they are absent, but these are few and very far between. Radiation is a most frequent attendant to the initial site of pain and tenderness; the following observations having been made in our series.

The initial site of both pain and tenderness has been in the right lower abdominal quadrant in 68 cases; in the periumbilical 42; diffuse, 34; in the left lower quadrant, 12; in the right upper quadrant, 4; in the left upper quadrant, 1, and in the epigastrium, 1. As seen in Figure 4, the radiation to the right lower quadrant has been manifest in the vast majority of cases, though there are a few in which no such radiation has occurred. It is interesting to note that the lower left quadrant has been the primary site in 12 cases (Fig. 4).



PRIMARY PAIN and TENDERNESS WITH RADIATION

Figure 4

TABLE 4.—*Clinical Findings as an Aid to Diagnosis in Acute Mesenteric Lymphadenitis*

Rectal Tenderness	
Bilateral	17
Right	31
Left	3
	51
Masses	
By rectum	4
Abdominally	1
	5
Temperature	
To 100 F. incl.	56
100-101+F.	96
102+F.	41
No mention	6
W. B. C. Count	
Maximum 10,000	89
11,000-15,000	49
16,000 and over	34
Taken to operating room immediately	26

Rectal examination has been positive as to tenderness in 51 cases: bilateral, in 17; right, in 31, and left, in 3 (Table 4).

Masses were discovered by rectum in four patients and noted abdominally in one (Table 4). These findings concur in no respect with those of FitzGerald, who stated in his recent report that in 35 cases lymph nodes could be palpated through the abdominal wall. Weeder remarked that rectal tenderness on the right could at times be elicited, as well as enlarged lymph nodes felt.

A variance of opinion is noted as to the question of temperature. Weeder notes that it will vary from 98.3 to 100 F; FitzGerald states that in about half of the cases there is "an elevation of temperature"; Gross feels that "fever is low grade"; Young [20] believes that the "temperature tends to be higher than that found in early appendicitis," and Christopher speaks of "occasional fever varying from 100°-102°." Temperature findings in our cases are given in Table 4. In at least 90% of our cases the pulse has been high and out of all proportion to the temperature.

Is a white blood cell count of any value as an aid to diagnosis? Gross states that it is rarely over 10,000, and Weeder concurs with this. On the other hand, Christopher

believes that there is a moderate leukocytosis; this latter assumption has been given by others.

In our series of 172 cases (the remaining 26 were taken to the operating room immediately, and no blood examination was performed), 51.7% showed a maximum count of 10,000 or under; 27.8% showed 11,000-15,000, and 19.6% showed 16,000 and over.

From the above it may be seen that differences of opinion arise, and though 51.7% of our cases showed a maximum of 10,000 or under, it is not of too great diagnostic importance unless one is endeavoring to make a presumptive diagnosis between mesenteric adenitis and acute appendicitis, in the latter of which ordinarily there is a higher degree of leukocytosis (Table 4).

Diagnosis.—Is it possible to form a definite symptom-sign complex in many of the cases, or are the signs and symptoms so commonly noted in acute appendicitis that differentiation between the two diseases cannot be made? In evaluating this differentiation, it might be well to take up separately the history and signs and symptoms of the two, basing one's observations only on this particular series.

History

Though previous attacks are quite commonly noted in acute appendicitis, acute mesenteric adenitis overbalances to a great degree those found in the history of acute appendicitis. One hundred nine of our series presented this history.

Duration

Too much stress cannot be thought of in the differentiation, with this exception—that it is extremely rare and only in neglected cases that the duration goes into days and perhaps weeks. Our series show that in 29 cases the duration was from 3 to 7 days, in 8 cases from 8 to 14 days, and in 7 cases from 15 to 30 days. This in itself is not foolproof but is worthy of consideration (Fig. 2).

Onset of the Attack

Usually in acute mesenteric adenitis the onset of the attack is not so sudden as in acute appendicitis and is frequently ushered in, before the pain begins, by malaise, headache, dizziness, anorexia, and perhaps head cold or other respiratory affections; a slight fever is often present. In this series the above symptoms were quite prominent.

The question usually arises as to whether or not the patient should be operated upon for the removal of the appendix, a differentiation between acute appendicitis and acute mesenteric adenitis not having been made.

Delay is not justified if the diagnosis of appendicitis has been made or when a definite diagnosis has not been formulated; as Gross states, "If any reasonable suspicion persists about the possibility of appendicitis, laparotomy should be undertaken."

On the other hand, I agree with Gross, who emphatically says that "several hours' delay in making observations will usually do no harm, even if appendicitis is present, and a number of useless laparotomies can be avoided thereby." This is especially true when one considers that in this disease there is a rapid subsidence of symptoms and findings, a course which is observed often in this condition (Adams). Avid [4] comments: "If the condition is mistaken for acute appendicitis, as it frequently is, no great harm is done. It may be worse to sacrifice accuracy for safety." Young emphasizes this when he states, "If the patient is very acutely ill and the differentiation from appendicitis cannot be made, certainly the safer plan is to operate."

If the patient is operated upon and enlarged nodes are noted, I believe that excision of a node is contraindicated, owing to its inflammatory condition and the result therefrom in the surrounding tissues.

In discussing primary acute mesenteric lymphadenitis, one should not overlook the possibility of the existence of tuberculous adenitis. Some years ago the latter affection was especially emphasized when a discussion

of mesenteric adenitis arose. Indeed, in 1931 Strömbeck,[15] of Sweden, presented a very extensive monograph on mesenteric lymphadenitis, though it dealt especially with tuberculosis of the mesenteric lymph nodes; he did, however, include in his report 14 cases of nontuberculous conditions in which the histologic examination showed "10, acute adenitis; 3, lymphoid hyperplasia, and 1, purulent inflammation." He noted that this affection (tuberculosis) could be diagnosed "almost to the same extent as by carefully made autopsies." I have very carefully reviewed the large array of cases presented by Strömbeck and have concluded that in the final analysis the text applied most especially to the differentiation between chronic appendicitis and tuberculous lymphadenitis. Great stress was put upon the roentgenographic findings of calcification in the mesenteric nodes, and, as Caffey[5] expressed it, "Calcifications in the abdominal nodes are almost exclusively tuberculous in origin." In hundreds of radiograms taken as routine in the Albany Hospital, it has been the very rare exception that calcification of the mesenteric lymph nodes was found. I feel that primary acute mesenteric lymphadenitis is a definite entity and that under ordinary conditions a tuberculous process should be considered only as a mere possibility.

Conclusions based upon a survey of the 198 cases may be summarized as follows.

1. The sign-symptom complex, as noted by various authors, is far from a uniform nature, and this is supported by our findings, which in themselves are far removed from the observation of many.

2. At the present time the etiology of the disease is based entirely upon hypothesis, no causative factor occupying a more prominent place than another.

3. There is concurrence that respiratory tract infection is a most important factor or perhaps coincidence; that sex and age are in accordance with one another; that guarding or voluntary rigidity is markedly commoner than base rigidity; that tenderness and pain are more marked in the right lower quadrant than in any other quadrant; that the temperature and leukocyte count are of no diagnostic importance, and that a seasonal factor or allergy is no factor.

4. There may be in exceptional cases a sign-symptom complex so worthy of consideration that surgical intervention is unnecessary. This would be based upon the following: a history of malaise; anorexia; previous similar attacks; no definite abdominal true splinting, and, above all others, such *symptomatology appearing in a young child.*

5. With the above sign-symptom complex, the patient need not be taken immediately to the operating room but should be observed for a few hours before a final decision is made.

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Heel Spur (Calcaneal Spur)

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Heel spur is an osteophytic outgrowth just anterior to the tuberosity of the calcaneus, extending along its entire width or about 2 to 2.5 cm. The apex of the spur is embedded in the plantar fascia directly anterior to its origin. The condition may exist without producing symptoms, or it may become very painful, even disabling.

Calcaneal spurs are of three types:

1. Those which are large in size but symptomless, because the angle of growth is such that the spur does not become a weight-bearing point and/or the inflammatory changes have been arrested. This type is usually found incidentally when the foot is x-rayed for some other purpose.

2. Those which are of large size and painful upon weight-bearing, because the pitch of the calcaneus has been altered by a depression of the longitudinal arch and, as a result, the spur may become a weight-bearing point, sometimes causing intractable pain (Figs. 13*A* and 14*A*).

3. Those which have only a rudiment of proliferation and whose outline is irregular and jagged, usually accompanied by an area of decreased density around the origin of the plantar fasica, indicating a subacute inflammatory process (Fig. 1). All calcaneal spurs undoubtedly begin in this manner, but only a few become symptomatic at this stage, because only in these few are the etiologic factors acute.

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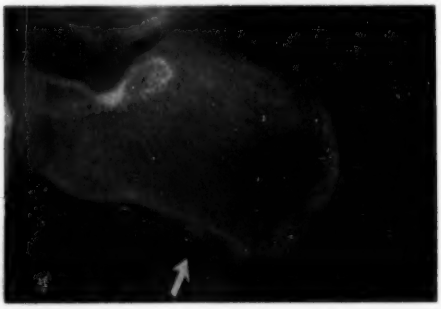
From the Department of Surgery, Columbus Hospital.

Fig. 1.—Spur formation with subacute fibrositis.



Etiology

The cause of heel spurs was long obscure, because it was generally believed that they were due to gonorrheal infection (gonorrheal spurs), as demonstrated by Baer,[1] Barker,[2] Holzapfel,[3] Swett,[4] and others. Von Lackum and Palomeque[5] were among the first to call attention to the fact that "gonorrheal spur is a misnomer." As late as 1932 Liberson[6] began his article with "the painful heel of gonorrhea is due to both bony exostosis and the soft tissue infiltration over it." Later writers suggested infectious diseases and trauma as causes of the spur formation. Blokhin (1937),[7] reporting 33 cases, found that arteriosclerosis, gonorrhea, and syphilis played no part in the cause, but rather it was the result of a functional overuse and/or an abnormality of the bones of the foot. Costa Bertani (1939)[8] found in 18 cases that heel spur occurred in 40% of patients with flatfoot. Winsett (1939)[9] claimed that heel spur was related to trauma occurring in conjunction with focal infection of some remote area. More recently Davis and Blair (1950)[10] reported 15 cases of spurs of the calcaneus in Strümpell-Marie disease. Heredity has been suggested as a factor by one writer. Gould (1942)[11] reported exostosis of the heel in a man who had six children; the third child, a son, had a spur. This son had four children, and the second child, a boy, had a heel spur. Gould suggested that the

abnormality passed down through the male side.

Twenty-five years ago I became aware of the marked discrepancy in the old gonorrheal theory. I noted that these patients were generally middle-aged, stout, stocky persons. The women were often of foreign birth and mothers of large families, the type least likely to have been afflicted with a venereal disease. In my series of 37 cases there have been about an equal number of men and women, ranging in age from 37 to 61 years. The women were all of average height but overweight, ranging from 170 to 315 lb., the majority over 200 lb. Of the men 70% were stocky and overweight; 30% were of normal weight. Many of these patients had a marked pes planus and some eversion of the foot.

The important factor in the cause is undoubtedly mechanical rather than infectious, and the result of the following chain of events.

The plantar fascia arises from the anterior lip of the tuberosity of the calcaneus, which is about 2 cm. wide. From this origin it fans out over the entire plantar surface of the foot and is inserted into the fascial plane under the five metatarsal heads, measuring at its insertion about 10 cm. in width (Fig. 2). The plantar fascia functions as a bowstring for the entire plantar surface of the foot; as a result any excess strain on the longitudinal arch exerts a maximum pull or strain at the acute angle of its origin. It can be readily seen that "weak foot" and overweight, which alters the pitch of the calcaneus, are important factors in producing such excess strain. Over a long period of time this produces a low-grade inflammatory process at this area (the origin of the fascia), resulting in secondary proliferation, ultimately forming the spur.

Fig. 2.—*A*, note the relative width of the plantar fascia at its origin and insertion. *B*, the bowstring action of the fascia.

Diagnosis

The principal symptom is severe pain in the entire plantar surface of the heel, which is aggravated by weight-bearing, becoming progressively worse and often incapacitating. Upon palpation, the entire plantar surface of the heel is tender, but the point of maximum tenderness will be elicited just anterior to the calcaneal tuberosity. Pinpointing this point of maximum tenderness on a radiogram will usually locate it immediately under the spur.

In the early stages the pathologic changes are a fibrositis of low chronicity with, or without, pain anterior to the calcaneal tuberosity. Continuation of the process produces osteophytic changes and bone deposits in the sulcus just anterior to the tuberosity. The accumulation of new bone is self-limiting, and the final spur may vary greatly in size and shape. The commonest shape of the entire spur is that of a triangular bar. The usual medial lateral view on a radiogram is two dimensional and leaves the impression that the spur is pointed like a tack, whereas it actually transcends the entire width of the tuberosity (Fig. 3).

Treatment

The asymptomatic case (Type 1) needs no attention. Most of the fully formed, symptomatic spurs respond to mechanical measure, such as proper footgear, correction

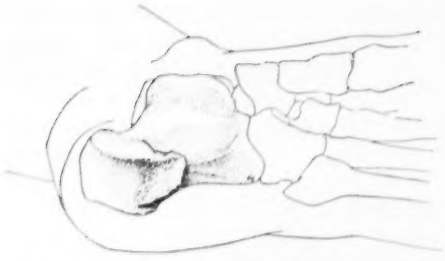


Fig. 3.—The spur transcends across the entire tuberosity of the calcaneus.

of any static foot disability, increased rest of the foot, and an appliance which will have a transverse sulcus in its heel portion to accommodate the spur. In the intractable case (Type 2) surgical excision of the spur is indicated. For the third type described, medical and mechanical measures should be thoroughly exhausted before surgical intervention is contemplated, because at this stage of active fibrositis palliative measures are more likely to arrest the disease and surgical intervention may only aggravate the problem.

A number of operative procedures have been devised in the treatment of heel spurs. Steindler's [12] rotation osteotomy (Fig. 4) of the calcaneus is designed to take all the weight-bearing off the point of the spur by rotating the posterior portion of the calcaneus in such a manner that the spur comes to lie in the horizontal plane and not in a vertical or oblique plane. The Steindler technique is as follows: A curved incision beginning on the lateral aspect of the foot, 1 in. above the insertion of the tendo Achillis, follows the tendo Achillis, then curves anteriorly and posteriorly and terminates at the lateral margin of the sole anterior to the tuberosity of the calcaneus. After exposing the calcaneus, the periosteum is stripped away, exposing the entire posterior and inferior portion of the calcaneus. A curved osteotomy through the calcaneus is then performed, the line of osteotomy passing from a point anterior to the insertion of the tendo Achillis to a point just anterior to the insertion of the plantar fascia at the tuberosity. The plane of the osteotomy is at right angles to the lateral surface of the calcaneus.

After removing a wedge from the inferior surface of the anterior portion of the calcaneus, the tendo Achillis is lengthened, and then the posterior portion of the calcaneus, carrying the spur with it, is rotated anteriorly and superiorly into its new position. An ivory bone peg or steel pin is used to hold the posterior portion in place, thereby bringing the spur into the horizontal plane.

Another procedure is that of Griffith [13] and of Chang [14] which is commonly practiced. A U-shaped incision is made com-

Fig. 4.—Steindler's rotation osteotomy for calcaneal spurs.

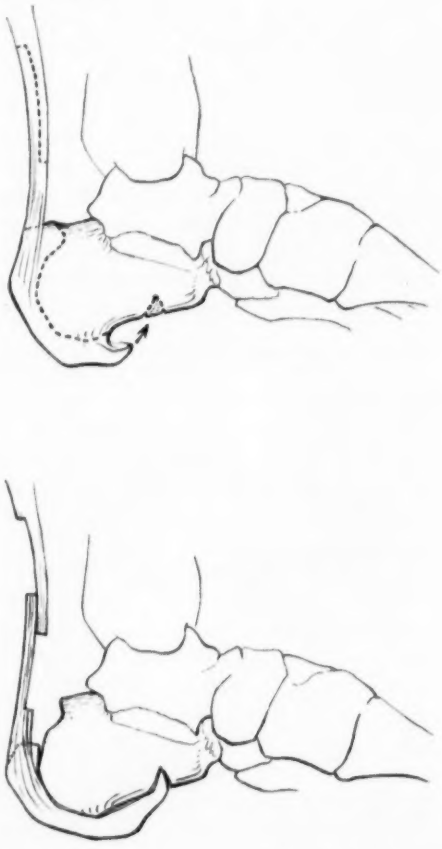


Fig. 5.—U-shaped flap approach for calcaneal exostectomy.

pletely around the heel; the skin flap is reflected, exposing the plantar surface of the heel at the origin of the plantar fascia (Fig. 5). The fascia is severed at its origin, followed by amputation of the spur.

Blokhin,[7] of Moscow, reported 33 cases in which he used a modified Chang technique and was successful in the 17 patients followed up after one to four years. A U-shaped incision was made in the skin around the heel "along the line where this skin changes into the thicker plantar skin." The flap of skin with the adhering layer of fat was lifted toward the sole in such a manner as to expose the lower surface of the calcaneus. The bursa of the tendon calcaneus was excised and the plantar fascia and muscles detached. The lower plantar tuberosity of the calcaneus was smoothed as much as possible with a chisel, and the same done with the periosteum and spur. The fascia was sutured with absorbable surgical suture to the subcutaneous cellular tissue of the flap of skin, which was then put back in place and sutured. Blokhin claimed that a lateral incision does not permit good access or good examination of the affected area and, because of insufficient radical surgery, may result in a recurrence.

All the above procedures are unnecessarily mutilating.

Surgical Procedure

In my 37 cases, in which surgery was clearly indicated, the following procedure was used without a single recurrence or residual disability. Success was probably due to the fact that the procedure is comparatively atraumatic, and the resulting scar formation at the origin of the plantar fascia has more tensile strength than the normal anatomic attachment of this fascia; as a result this scar tissue is able to withstand more stress than normally.

1. A linear incision is made over the medial side of the calcaneus about 2 cm. above the plantar border (Fig. 6). This is usually immediately over the medial border of the plantar fascia. The incision is begun at about the posterior border of the calcaneus and continued to about the anterior third of this bone. The entire incision need be no longer than 5 to 6 cm. The spur will now be immediately under and in the middle of the incision.

2. The incision is continued in depth until the medial border of the plantar fascia is exposed. The index finger of the right hand is placed over the superior surface of the plantar fascia just anterior to its origin, and an attempt is made to free it completely across to the lateral side (Fig. 7). Dissection with scissors is continued to free the fascia over and around the spur until it is completely denuded on its superior and inferior surfaces across from the medial to the lateral side (Fig. 8).

3. With the blade of an 8 mm. Andrew's mastoid osteotome placed against the base of the spur, the pressure of the palm of the right hand against the osteotome is suffi-

Fig. 6.—A linear incision, about 6 cm. long, is made on the medial side about 2 cm. above the medial plantar border of the skin.

Fig. 7.—The index finger is able to free the space immediately above the plantar fascia and the apex of the spur.

Fig. 8.—With scissors all the integument is freed from the spur.

cient to amputate the spur across the entire surface of its base (Fig. 9). The surface after the excision is smoothed with a Joseph nasal rasp (Fig. 10). The fascia and skin are sutured in layers (Fig. 11), and a compression bandage is applied; no other immobilization is required.

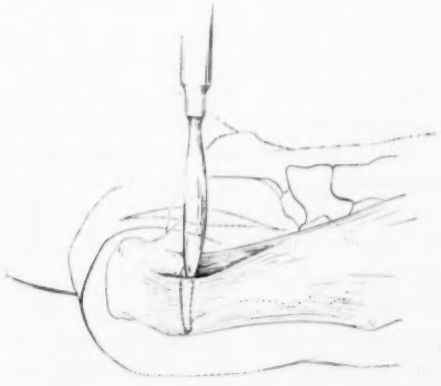
The patient may assume weight-bearing with the aid of crutches in about four days. Sutures are removed in 10 to 12 days. In about four weeks after the operation full weight-bearing may be resumed. A sponge-rubber mold, fashioned from a mold of the foot, will stabilize the foot and hasten recovery.

Prognosis

The advisability of surgical removal of spurs has been questioned by many, because it is claimed that the spur tends to recur. My personal experience does not coincide with this opinion, and I fail to find evidence in the literature to support such contention. Such evidence would require a series of cases where comparison of preoperative, immediately postoperative, and late postoperative roentgenograms demonstrates the recurrence of the spur. Certainly some roughening of the bone at the point of amputation of the spur does form in some cases; however, I have not seen a single

Fig. 9.—With an 8 mm. osteotome the spur is amputated.

Fig. 10.—The surface of amputation is smoothed with a Joseph nasal rasp.



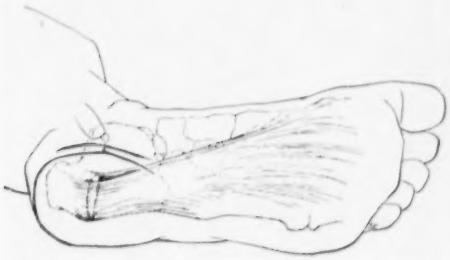


Fig. 11.—The fascia and skin are closed in layers.

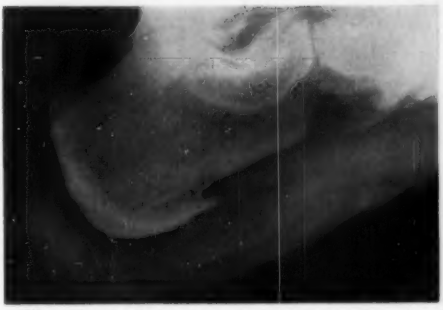


Fig. 12.—A "recurrent spur," showing roughening on the plantar tuberosity of the calcaneus and the cortex of the spur perfectly smooth.

case where this roughening became symptomatic. I have seen two cases, both supposedly having had spurs removed earlier, which showed the spur as smooth in outline as any preoperative spur; yet the plantar tuberosity of the calcaneus was roughened as though it had been chisled upon (Fig. 12). Evidently the operator had missed the spur and removed part of the tuberosity, thereby causing a roughened surface. The spur which was present could not be a recurrent spur, for, if recurrent, the spur's cortex would have been rough. I removed the spur in each of these two patients, and there has been no recurrence after 15 years.

Report of Two Cases

Case 1.—This woman, a housewife, age 44, 5 ft. 4 in., weight 209 lbs., complained of intractable pain under both heels which was not relieved by numerous appliances and courses of physical therapy. Physical examination and routine laboratory findings were negative.

Roentgenograms revealed bilateral calcaneal spurs (Fig. 13*A*). On July 13, 1953, the spurs were excised by my procedure. The patient made an uneventful recovery and has been free from pain in her heels ever since; Figure 13*B* is a view taken of this patient on March 3, 1956.

Case 2.—This man, an attorney, age 55, height 5 ft. 10 in., weight 267 lb., complained of pain in both heels which had not responded to mechanical or physical therapy. Physical examination and routine laboratory findings were negative. Roentgenograms revealed bilateral calcaneal spurs (Fig. 14*A*). On Nov. 11, 1953, the spurs were excised by the above procedure. The patient made an uneventful recovery, except for a severe reaction to a prophylactic dose of penicillin. He was seen March 15, 1956 (Fig. 14*B*), completely free from pain in his heels.

I have seen many patients as long as 20 years after surgery for calcaneal spur; all are completely free from pain in the heel.

I know of no case in my series which had a recurrence of symptoms.

Fig. 13A (Case 1).—Calcaneal spur.

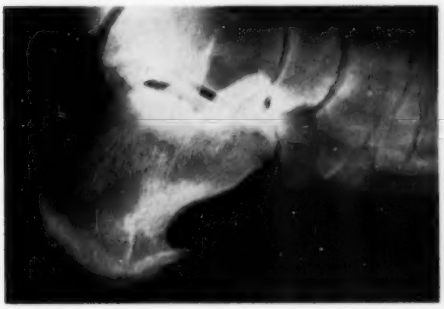


Fig. 13B (Case 1).—Three years after operation.

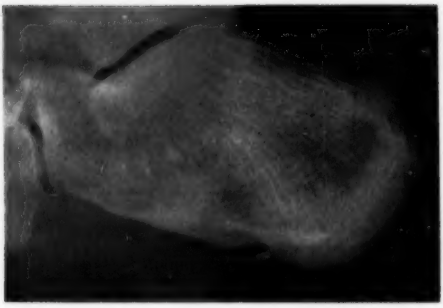


Fig. 14A (Case 2).—Calcaneal spur.

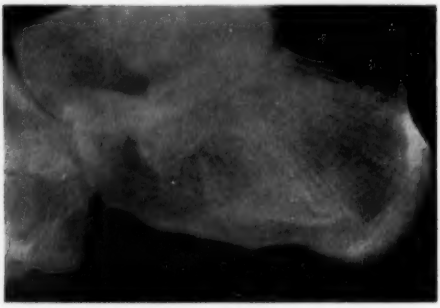


Fig. 14B (Case 2).—Three years after operation.

Summary

Heel spur is due to mechanical, rather than infectious, factors.

Three types of heel spur are described.

Surgery is indicated only after palliative measures have failed.

The surgical technique described has proved permanently successful in a series of 37 cases.

25 E. Washington St. (2)

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Hemangioma of the Liver

Report of a Case with Resection of the Left Hepatic Lobe

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Hemangioma occurs in the liver more frequently than in any other internal organ. The diagnosis of hemangioma of the liver is seldom made preoperatively. An epigastric mass is usually noted first, which may or may not be accompanied by mild indigestion, pain, fullness after eating, or even jaundice.[1-4] Most symptoms are nonspecific and probably related to pressure. Cecil [5] presents a patient who had intermittent obstructive symptoms due to a large hemangioma pressing on the cardiac end of the stomach.

Complications of the hemangioma have been reported. Spontaneous rupture has been reported in adults [6] and in infants.[7] These tumors are quite friable, and simple biopsy is dangerous.[3] One case of continued, uncontrollable, and fatal hemorrhage from a biopsy site in a hemangioma has been reported.[4] The lesion is a vascular one in an extremely vascular organ, and the danger of hemorrhage from the tumor is certainly great.

The problem of treatment of these tumors is a speculative one. If the tumor is easily resectable, it probably should be removed because of the potential hazards of trauma and bleeding. Nonresectable tumors have been treated with x-ray with good results.[8-10] Ray [10] placed four silver clips at the periphery of a nonresectable hemangioma of the liver and treated the patient with x-ray. He followed the size of the tumor roentgenologically by taking serial views of the abdomen which showed the clips. The projected size of the tumor diminished gradually.

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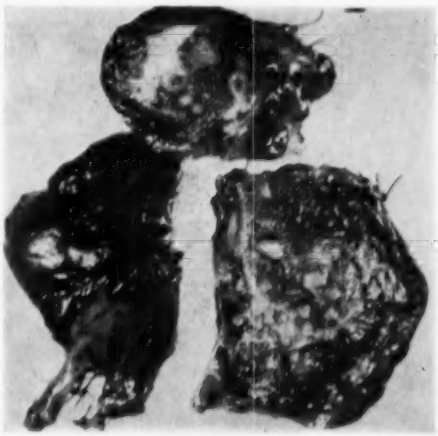
From reported cases it would seem that excision of the hemangioma, when feasible, would be the most efficacious. There has been only one death reported following resection,[3] while many extensive resections have been successfully performed.[1-3,5,11-24]

Extensive liver resection can be safely performed, and no deleterious effects have been noted. The case herein reported represents a left hepatic lobectomy for a large hemangioma involving the entire left lobe of the liver.

Report of Case

A 26-year-old housewife was first seen in December, 1955, complaining of pain and discomfort in the left upper abdomen. She noted nausea but no vomiting. She noted some intolerance to fried and greasy foods. The pain seemed to radiate upward. She had been examined four years previously and was told that she might have an enlarged liver. During the four years prior to

Fig. 1.—Gross specimen, showing cut surface of left lobe of liver and nodular appearance of external surface.



examination the pain and discomfort had been troublesome. Her appetite had been poor during the past four years, and she noted much gas.

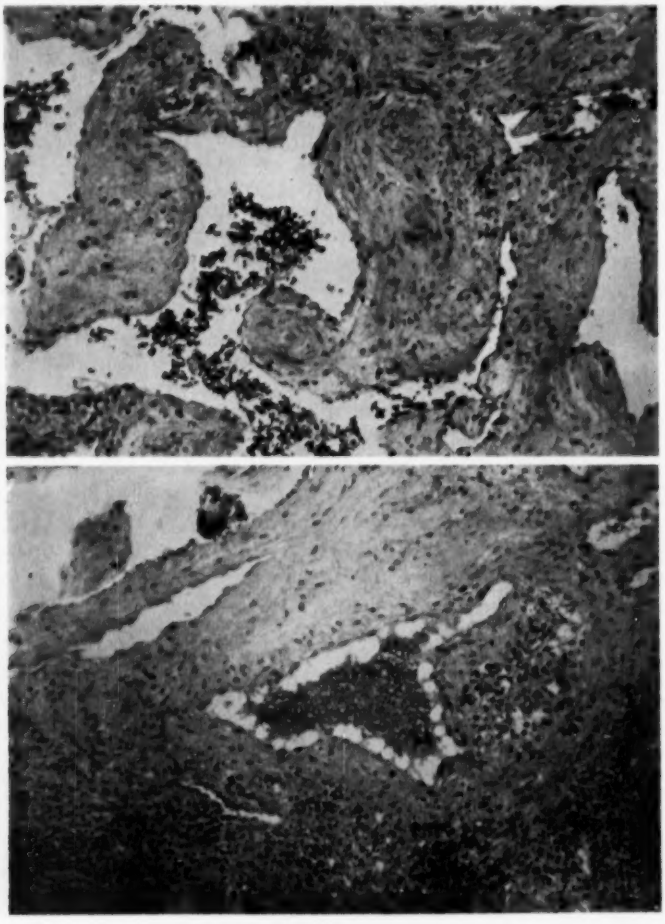
Physical examination was not remarkable except for a firm mass in the upper abdomen, extending below the sternum for the distance of about 5 cm. It was nontender, with a rounded smooth border rather than a sharp one. On inspiration it descended. When the patient turned on her left side, the mass moved to the left subcostal region, and the margin could be differentiated from the liver.

Oral cholangiography was normal. X-ray examination of the upper gastrointestinal tract was done and showed slight compression of the stomach by this mass. Barium enema was normal.

Preoperative diagnosis was leiomyoma of the mesentery of the stomach or possible splenomegaly.

Operative Note.—Operation was conducted on Dec. 30, 1955. On exploring the abdomen, it was immediately noted that the mass was a huge hemangioma involving the entire left lobe of the liver. There were several small hemangiomas in the right lobe. The coronary ligament, extending from the left lobe to the diaphragm, was cut, reflecting the left lobe downward. The round ligament and the falciform ligament were also cut and ligated. The left hepatic artery and vein were isolated, ligated, and divided. Mattress sutures were placed across the junction between the right and left lobes, and the left lobe resected behind these hemostatic sutures. The falciform ligament was placed over the cut edge of the liver and sutured in place. The wound was drained. The patient lost a minimal amount of blood during the procedure.

Fig. 2.—Photomicrographs, showing irregular cords of fibrous connective tissue covered by a layer of endothelial-type cells.



After the operation the patient did well. Liver function studies included BSP, bilirubin, prothrombin, and serum protein, and all were within normal limits. The patient was discharged from the hospital on Jan. 9, 1956. She has since been followed as an outpatient and in December, 1956, was doing well. She does her own housework, cares for two children, and is symptom-free.

Pathologist's Report.—Gross specimen consists of 270 gm. of liver, measuring 11 by 9 by 6 cm. and having a closed line of sutures at the one edge. The mass is very soft and does not have the consistency of liver, although it has the color. On section, the architectural pattern is distorted. There is no normal liver tissue seen. The tissue, on the whole, has more the appearance of lung than liver (Fig. 1).

Microscopic: Tissue from the liver shows irregular cords of fibrous connective tissue which are covered on all sides by a single layer of endothelial-type cells. The spaces between these cells contain blood cells and a few white cells. These spaces form confluent caverns which are filled with blood. There is some normal liver tissue present, which shows a rather marked leucocytic infiltration. This represents a massive benign cavernous hemangioma of the liver. (Fig. 2).

In this case the left lobe of the liver was completely involved with the hemangioma. Resection of the left lobe was easily accomplished by using mattress sutures of the absorbable surgical suture variety. Blood loss was minimal. Certainly resection of the mass is preferable to x-ray treatment when it is technically feasible.

Summary

A case of hemangioma of the left lobe of the liver is presented.

The left lobe was resected without difficulty, removing the entire hemangioma.

Mr. John Ford assisted with the photomicrography, and Melvin Oosting, M.D., prepared the pathology reports.

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Partial Gastrectomy *versus* Vagotomy with Gastroenterostomy in Treatment of Duodenal Ulcer

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Introduction

The relative merits of partial gastrectomy *vs.* vagotomy with gastroenterostomy in the definitive surgical treatment of duodenal ulcer remain a controversial subject at the present time.

During the period 1946-1954, a total of 348 patients with duodenal ulcers were subjected to partial gastrectomy (Billroth II type) and 178 patients with duodenal ulcers were subjected to vagotomy with gastroenterostomy on the surgical services of the Hines Veterans' Administration Hospital and the University of Illinois Research and Educational Hospital. It is the purpose of this paper to present the findings noted in a comparative evaluation of these two groups of patients.

Age Distribution

The age distributions of the two groups of patients are tabulated in Table 1. The percentage of patients in each decade was roughly comparable for the two types of operation. Although vagotomy with gastroenterostomy was utilized in five of six patients 70 years of age or older, the percentage of patients 60 years of age or older treated by each operative method was the same (13.5%).

Previous Perforation

There was a history of perforation of duodenal ulcer in 64 of the 348 patients subjected to partial gastric resection (18.4%) as compared with a similar history in 41 of 178 patients subjected to vagotomy with gastroenterostomy (23.0%). Nine of the patients (2.6%) subjected to partial gastrectomy had a history of two episodes of perforated duodenal ulcer as compared with five patients (2.8%) in the group subjected to vagotomy with gastroenterostomy.

Principal Indication for Surgery

In Table 2 tabulation of the principal indication for surgery in each patient is presented for the two types of operation. Obstruction and pain were the commonest indications for surgery in both the partial gastrectomy group and the vagotomy with gastroenterostomy group. However, in the partial gastrectomy group hemorrhage (acute or chronic) constituted the principal

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TABLE 1.—*Age Distribution*

	Partial Gastrectomy (348 Cases)		Vagotomy with Gastroenterostomy (178 Cases)	
Age	No.	%	No.	%
20-29	48	13.8	16	9.0
30-39	67	19.3	38	23.3
40-49	51	14.7	37	20.8
50-59	135	38.8	63	35.4
60-69	46	13.2	19	10.7
70 +	1	0.3	5	2.8

TABLE 2.—*Principal Indication for Surgery*

	Partial Gastrectomy (348 Cases)		Vagotomy with Gastroenterostomy (178 Cases)	
	No.	%	No.	%
Hemorrhage (acute)	54	15.5	0	----
Hemorrhage (chronic)	53	15.2	4	2.3
Obstruction	127	36.5	80	44.9
Pain	110	31.6	94	52.8
Perforation	1	0.3	0	----
Miscellaneous	3	0.9	0	----

indication for surgery in an appreciable number of patients (30.7%).

Estimated Amount of Gastric Resection

Since the operations were performed by a large number of attending surgeons (or by their residents), with varying philosophies as to the amount of stomach which should be removed in order to adequately control the ulcer diathesis, there was no consistent uniformity in the extent of gastric resection. In Table 3 are listed the estimated amounts of gastric resection in the 348 patients subjected to partial gastric resection, as specifically stated in the surgeons' dictated operative record. No attempt was made by us to interpret the amount of resection from anatomical landmarks, etc., in those records in which the surgeon did not specifically estimate the percentage of stomach removed. Most of the patients in whom an estimate was made were estimated to have had two-thirds or more of the stomach removed. Since most of these estimates apparently were based on subjective impressions of the surgeon rather than on any objective criteria, the accuracy of such classification may be questioned, as the studies of Harkins and Moore [1,2] in recent years have established.

Postoperative Complications

The postoperative complications occurring in the two groups of patients are tabulated in Table 4. Since the incidence of postoperative complications may be directly related to the thoroughness with which they are diagnosed, fever of unknown origin is listed as a complication in those patients without a diagnosed complication in whom the postoperative temperature was elevated to102 F (rectal) or above, inasmuch as this fever was possibly related to an unrecognized complication.

TABLE 3.—*Estimated Amount of Gastric Resection* (348 Cases)

Resection	Patients, No.
1/2–2/3	56
2/3–3/4	102
3/4 or more	93
?	97

Of the 348 patients subjected to partial gastrectomy, 172 postoperative complications occurred in 131 patients (37.7%). Of the 178 patients subjected to vagotomy with gastroenterostomy, 66 postoperative complications occurred in 46 patients (25.8%). Thus, 62.3% (217 patients) of the partial gastrectomy group were without postoperative complications as compared with 74.2% (132 patients) of the vagotomy with gastroenterostomy group.

Wound complications occurred in approximately the same percentage of patients after partial gastrectomy and after vagotomy with gastroenterostomy. On the other hand, pulmonary complications were approximately three times commoner after partial gastrectomy (12.7% *vs.* 4.4%). However, postoperative abdominal complications were slightly commoner after vagotomy with gastroenterostomy (14.6% *vs.* 11.2%). The commonest abdominal complications after vagotomy with gastroenterostomy were diarrhea, gastric atony, and stomal obstruction. The commonest abdominal complication after partial gastrectomy, on the other hand, was duodenal stump leak (12 patients—3.5%). Cardiovascular complications were approximately twice as frequent in the vagotomy with gastroenterostomy group (5.2% *vs.* 2.4%); the differ-

TABLE 4.—*Postoperative Complications*

Complication	Partial Gastrectomy (348 Patients)		Vagotomy with Gastroenterostomy (178 Patients)	
	No.	%	No.	%
Wound				
Abscess or cellulitis	15	4.3	7	3.9
Dehiscence	10	2.9	4	2.2
Evisceration	3	0.9	1	0.6
Pulmonary				
Atelectasis	17	4.9	4	2.2
Bronchopleural fistula	1	0.3	0	----
Empyema	1	0.3	0	----
Pleural effusion	1	0.3	0	----
Pleuritis	1	0.3	4	2.2
Pneumonitis	22	6.3	4	2.2
Pulmonary edema	1	0.3		
Abdominal				
Cardiospasm	0	0.0	2	1.1
Diarrhea	5	1.4	6	3.4
Duodenal stump leak	12	3.5	0	----
Gastric atony	1	0.3	10	5.6
Gastric dilatation	1	0.3	0	----
Gastrointestinal bleeding	5	1.4	0	----
Pancreatic fistula	1	0.3	0	----
Pancreatin	1	0.3	0	----
Paralytic ileus	1	0.3	0	----
Stomal obstruction	7	2.0	8	4.5
Subphrenic abscess	7	2.0	0	----
Cardiovascular				
Cardiac decompensation	3	0.9	1	0.6
Myocardial infarct	1	0.3	1	0.6
Pulmonary embolus	2	0.6	0	----
Thrombophlebitis	8	2.3	7	3.9
Vascular collapse	1	0.3	0	----
Renal				
Acute glomerulonephritis	1	0.3	0	----
Anuria	1	0.3	0	----
Hepatorenal syndrome	1	0.3	0	----
Lower nephron nephrosis	1	0.3	0	----
Urinary tract infection	3	0.9	1	0.6
Fever of unknown origin (102 F [rectal] or above)	30	8.6	7	3.9
Miscellaneous				
Serum hepatitis	9	2.6	3	1.7

ence was largely due, however, to a higher incidence of thrombophlebitis in the patients subjected to vagotomy with gastroenterostomy. Few urinary tract complications were noted in the two series; however, they were found approximately three and one-half times more frequently in the partial gastrectomy series than in the vagotomy with gastroenterostomy series. Fever of unknown origin (102 F [rectal] or above) was noted twice as frequently in the postoperative course of the group of patients subjected to partial gastrectomy. Also, serum hepatitis was noted slightly more frequently in the group subjected to partial gastrectomy (2.6% *vs.* 1.7%), reflecting the greater use of blood transfusions in this group.

Postoperative Deaths

The postoperative deaths occurring after partial gastrectomy and after vagotomy with gastroenterostomy are tabulated in Tables 5 and 6. There was a postoperative mortality of 4.9% (17 deaths in 348 patients) after partial gastrectomy as compared with a postoperative mortality of 1.1% (2 deaths in 178 patients) after vagotomy with gastroenterostomy. However, the mortality after partial gastrectomy was 2.9% (7 deaths in 241 patients) when the indication for surgery was other than acute or chronic hemorrhage. Of the 17 postoperative fatalities after partial gastrectomy, death was secondary to duodenal stump leak in 7 cases. The principal causes of death for the other 10 postoperative mortalities after partial gastrectomy were bronchopneumonia or massive atelectasis (3 cases); vascular collapse (1 case); hepatorenal syndrome (1 case); pulmonary embolus (1 case); myocardial failure (1 case); myocardial infarct (1 case); gangrene of colon (1 case), and unknown (1 case). The principal causes of death in the two postoperative fatalities after vagotomy with gastroenterostomy were bronchopneumonia (1 case) and myocardial infarct (1 case).

TABLE 5.—*Deaths After Partial Gastrectomy*
(Seventeen in 348 Cases)

Case, No.	Age	Indication for Surgery	Principal Cause of Death	Contributing Causes of Death	Postop. Day of Death	Comments
1	29	Hemorrhage (acute)	Massive atelectasis	Serum hepatitis secondary to numerous transfusions 6 wk. prior to emergency surgery	6	Ulcer not removed; 1st day postop. reoperated for continued hemorrhage, and ulcer site oversewn
2	43	Hemorrhage (acute)	Peritonitis secondary to duodenal stump leak	(1) Lower nephron nephrosis (2) Localized pancreatic necrosis	3	No drains
3	60	Hemorrhage (acute)	Vascular collapse	Atelectasis of left lower lobe	4	Received 7,000 cc. blood preoperatively
4	56	Hemorrhage (acute)	Bilateral bronchopneumonia	----------	9	----------
5	51	Hemorrhage (acute)	Unknown	Wound dehiscence	45	Sudden death; cause not determined at postmortem examination
6	38	Hemorrhage (acute)	Peritonitis secondary to duodenal stump leak	Bronchopneumonia	11	Repair of perforated duodenal ulcer 21 days previously at another hospital; wound disrupted 6 days postop.; and massive bleeding began 10 days postop.; transferred after 21 days postop.; recurrent massive hemorrhages; received 31,000 cc. blood
7	56	Hemorrhage (acute)	Peritonitis secondary to duodenal stump leak	Bronchopneumonia; cardiac decompensation	6	No drains
8	59	Hemorrhage (chronic)	Peritonitis secondary to duodenal stump leak	Anuria secondary to blood transfusion reaction	9	No drains
9	49	Hemorrhage (chronic)	Peritonitis secondary to duodenal stump leak	----------	4	No drains
10	40	Hemorrhage (chronic)	Vascular collapse secondary to perforation of duodenal stump	----------	1	No drains
11	55	Obstruction	Heptorenal syndrome	(1) Pancreatic fistula (2) Wound dehiscence	12	Penrose drain
12	52	Obstruction	Bilateral bronchopneumonia	(1) Diarrhea (protracted) (2) Hepatitis (3) Wound dehiscence	11	----------
13	51	Obstruction	Pulmonary embolus	----------	13	----------
14	53	Obstruction	Peritonitis secondary to gangrene of right half of colon and perforation of cecum	Pneumonitis	19	Resection right half of colon with ileostomy and transverse colostomy 7th day postop.
15	29	Obstruction	Peritonitis secondary to duodenal stump leak	Hemorrhage from excluded ulcer	10	No drains
16	71	Obstruction	Myocardial infarct	(1) Wound dehiscence (2) Wound abscess (3) Bronchopneumonia (4) Empyema (5) Bronchopleural fistula	94	----------
17	59	Pain	Myocardial failure	(1) Lobar pneumonia (2) Localized peritonitis secondary to duodenal stump leak	8	No drains at operation; perforation of duodenal stump 2d day postop.; drains then inserted

Death secondary to duodenal stump leakage, the major cause of death after partial gastrectomy, occurred in 7 of the 12 patients of this series in whom a duodenal stump leak developed. It is important to note that in six of the seven fatalities drains had not been placed near the area of the duodenal closure at the time of operation. On the other hand, intraperitoneal drains (Penrose) had been utilized in all five of the nonfatal cases.

In four of the seven fatal cases no difficulty in closure of the duodenal stump was reported by the surgeon. Similarly, St. John and associates,[3] who have recommended routine placement of a drain near the site of the duodenal stump, noted that in none of the eight cases of duodenal leakage in their

TABLE 6.—*Deaths After Vagotomy with Gastrenterostomy*
(Two in 178 Cases)

Case, No.	Age	Indication for Surgery	Principal Cause of Death	Contributing Causes of Death	Postop. Day of Death	Comments
1	58	Obstruction	Bronchopneumonia	----------	20	Pneumonia began 8th day after operation
2	46	Pain	Myocardial infarct	----------	5	----------

series did the surgeon feel that the closure was insecure. Since back pressure from obstruction may cause leakage of even the most secure duodenal closure, we now also feel that it is safest to place drains near the site of the duodenal stump routinely at the time of gastrectomy. If multiple Penrose drains are utilized, as recommended by Reynolds,[4] rather than a single drain, there will be less tendency for the drainage tract to become sealed off and hence rendered ineffective. If duodenal drainage develops, more effective evacuation of the fluid can be obtained by introducing a sump drain or soft rubber tube into the drainage tract alongside the Penrose drains and by utilizing mild suction via a small electric motor pump.

Another routine precaution which we would advocate at the time of surgery is to thread the gastric suction tube through the stoma and into the afferent jejunum up proximal to the duodenojejunal junction. If additional holes are cut in the tube, suction will decompress both the stomach and the duodenum and thus obviate any back pressure upon the duodenal stump.

The one death in this series (Case 6) secondary to duodenal stump leakage despite the placement of Penrose drains occurred in a patient who was in extremely poor preoperative condition from two operations during the preceding three weeks at another hospital and from continuing acute hemorrhage. Duodenal closure was difficult, unsatisfactory, and recognized to be grossly inadequate at the time of surgery. Abdominal drainage was apparent within hours after operation. In retrospect it would have been wiser in this patient because of the pervious closure to have utilized the procedure of catheter duodenostomy with complementary catheter jejunostomy, as suggested by Welch.[5]

In Table 7 the postoperative mortalities after partial gastrectomy and after vagotomy with gastroenterostomy are correlated with the principal indication for surgery. Postoperative fatalities after partial gastrectomy occurred most frequently in the acute hemorrhage group (13.0%—7 of 54 patients) and the chronic hemorrhage group (5.7%—3 of 53 patients). However, since vagotomy with gastroenterostomy is not considered an effective method of treatment of acute hemorrhage from peptic ulcer and was utilized in the treatment of chronic hemorrhage in only a few instances in this series, comparison of mortality rates in this study is rational only between groups of patients in whom the principal indication for surgery was either obstruction or pain. In patients for whom the principal indication for surgery was obstruction, the postoperative mortality rate was 4.7% (6 deaths in 127 patients) after partial gastrectomy and 1.3% (1 death in 80 patients) after vagotomy with gastroenterostomy. In patients for whom the principal indication for surgery was pain, the postoperative mortality rate was 0.9% (1 death in 110 patients) after partial gastrectomy and 1.1% (1 death in 94 patients) after vagotomy with gastroenterostomy.

Recurrent Ulceration

Follow-up (one to eight years after operation) was obtained in 70.0% of the patients surviving partial gastrectomy and in

TABLE 7.—*Correlation of Postoperative Mortality with Indication for Surgery*

	Partial Gastrectomy (348 Cases)			Vagotomy with Gastroenterostomy (178 Cases)		
	Patients, No.	Deaths, No.	Mortality, per Cent	Patients, No.	Deaths, No.	Mortality, per Cent
Hemorrhage (acute)	54	7	13.0	0	--	--
Hemorrhage (chronic)	53	3	5.7	4	0	0.0
Obstruction	127	6	4.7	80	1	1.3
Pain	110	1	0.9	94	1	1.1
Perforation	1	0	--	0	--	--
Miscellaneous	3	0	--	0	--	--

74.4% of the patients surviving vagotomy with gastroenterostomy.

There were five cases of recurrent ulceration proved at surgery and/or by roentgenogram in the 231 patients followed after partial gastrectomy (2.2%). There were also four cases of presumptive recurrent ulceration (hematemesis and/or characteristic ulcer pain) after partial gastrectomy (1.7%). Thus, at the time of follow-up there was a recurrence rate (proved and presumptive) of 3.9% after partial gastrectomy. The extent of gastric resection in these nine patients was estimated by the surgeon to be 75% (one patient); 70% (two patients); 65% (one patient); 60% (three patients), and not estimated (two patients). Thus, in only one of the cases with recurrent ulceration did the surgeon estimate that a 75% resection had been performed. (Wangensteen's clinic, which is one of the leading advocates of 75% resection, has reported a recurrence rate of approximately 1.6% in a large series of patients.[6])

During a comparable period of follow-up there were 10 cases of recurrent ulceration proved at surgery and/or by roentgenogram in the 131 patients followed after vagotomy with gastroenterostomy (7.6%). In addition, there were seven cases of presumptive recurrent ulceration (hematemesis and/or characteristic ulcer pain) after vagotomy with gastroenterostomy (5.3%). Thus, at the time of follow-up there was a recurrence rate (proved and presumptive) of 12.9% after vagotomy with gastroenterostomy.

Oberhelman and Dragstedt[7] have reported a proved recurrent ulceration rate of 5.8% and a presumptive recurrent ulceration rate of 1.4% (total recurrence rate of 7.2%) in 487 patients with duodenal ulcer treated by vagotomy with gastroenterostomy in Dragstedt's clinic. On the other hand, Crile,[8] who has been an advocate of vagotomy with gastroenterostomy, has reported a proved recurrent ulceration rate of 8% and a presumptive recurrence rate of 9% (total recurrence rate of 17%) in 145 cases followed five to eight and one-half years after vagotomy with gastroenterostomy.

Oberhelman and Dragstedt have reported that in their experience recurrent ulceration following vagotomy with gastroenterostomy has usually occurred in patients with incomplete vagotomy or in patients who develop persistent stasis of food in the stomach because of improper placement of the gastroenterostomy stoma. Since many of the operations reported in this paper were performed before the importance of antral placement of the gastroenterostomy had been established by the experimental and clinical evidence of Dragstedt and co-workers, it is not unlikely that more distal placement of the gastroenterostomy stoma in some cases might have materially reduced the recurrence rate. However, of the 28 recurrences (5.8%) reported by Oberhelman and Dragstedt, only 8 were associated with improper position of the gastroenterostomy stoma, and 20 recurrences (4.1%) were apparently attributed to incomplete vagotomy. It would not seem unreasonable to suspect that the incidence of incomplete vagotomy (and consequent possible recurrent ulceration) would be appreciably greater in the hands of others less experienced and skilled in the performance of vagotomy than the surgeons of Dragstedt's clinic.

The possibility of incomplete performance of vagotomy in at least 4% (and possibly more) of patients constitutes a technical liability to the effectiveness of vagotomy with gastroenterostomy. On the other hand, subjective estimation of the extent of the gastric resection all too frequently may be based on wishful thinking by the surgeon, as mobilization of the stomach becomes more difficult and militates against accurate clinical evaluation of the effectiveness of the various percentage gastric resections. However, objective measurement of the extent of gastric resection by simple methods will eliminate this technical source of error.[1,2,9] Another technical factor which could limit the theoretical effectiveness of

partial gastrectomy is incomplete removal of the antral mucosa in patients in whom the antrum is retained, because it is not technically feasible or safe to remove the ulcer. However, if the antral mucosa is carefully removed to the pyloric ring, this possible liability to recurrence can be alleviated. Nevertheless, we feel that the technical factors which might hinder the performance of a technically perfect partial gastrectomy are more susceptible to control by the surgeon than is the main factor (anatomic arrangement of the vagus nerves) which might affect the performance of a technically perfect vagotomy.

Weight Status

Comparison of weight at the time of follow-up with preoperative average healthy weight was obtained in 222 patients after partial gastrectomy and in 118 patients after vagotomy with gastroenterostomy (Table 8). In this comparison 14.9% of patients subjected to partial gastrectomy and 15.3% of patients subjected to vagotomy with gastroenterostomy were above their preoperative average healthy weight at the time of follow-up, with an average gain of 10 lb. and 14 lb., respectively. However, 78.8% of patients with partial gastrectomy and 71.2% of patients with vagotomy and gastroenterostomy were below their average healthy weight, with an average loss of 17 lb. and 16 lb., respectively. Similarly, no significant difference was noted in the percentage of patients with appreciable weight losses after partial gastrectomy *vs.* vagotomy with gastroenterostomy.

The Dumping Syndrome

The incidence of the dumping syndrome was also ascertained in 222 patients after partial gastrectomy and in 118 patients after vagotomy with gastroenterostomy. The diagnostic symptoms of the dumping syndrome were considered in this study to be weakness, sweating, or dizziness occurring during a meal or within one hour after the meal. The presence of any of these symptoms, even to a slight degree, as established by direct leading questions, was accepted as evidence of the presence of the dumping syndrome.

At the time of follow-up the dumping syndrome of some degree was noted to be present in 50.8% of the patients studied after partial gastrectomy and in 52% of the patients studied after vagotomy with gastroenterostomy. Hence, in this study no significant difference was noted in the incidence of the dumping syndrome after partial gastrectomy and after vagotomy with gastroenterostomy.

Patient Satisfaction

Of surviving patients, 92.6% studied after partial gastrectomy and 84.0% studied after vagotomy with gastroenterostomy were satisfied with the results of their respective operations at the time of follow-up study. Patient dissatisfaction with the operative result was most commonly associated with the presence of the dumping syndrome, recurrent ulceration, or appreciable weight loss.

TABLE 8.—*Weight Changes After Partial Gastrectomy and After Vagotomy with Gastroenterostomy for Duodenal Ulcer*
(Comparison with Average Healthy Weight)

	Partial Gastrectomy Patients, No.	Vagotomy with Gastroenterostomy Patients, No.
Total no. of patients	222	118
Weight gain	33 (14.9%)	18 (15.3%)
No weight change	14 (6.3%)	16 (13.6%)
Weight loss	175 (78.8%)	84 (71.2%)
10 lb. or more	101 (45.5%)	55 (46.6%)
20 lb. or more	57 (25.7%)	23 (19.5%)
30 lb. or more	23 (10.4%)	12 (10.2%)

However, if patients who expired in the postoperative period are included among the dissatisfied patients (which they obviously must be), the patient satisfaction after partial gastrectomy is reduced to 86.3% as compared with 82.7% after vagotomy with gastroenterostomy. Thus, the over-all percentage of patient satisfaction (including postoperative deaths) probably is not significantly different for the two operations.

Summary and Conclusions

A comparative study was made of 348 patients with duodenal ulcers subjected to partial gastrectomy and 178 patients with duodenal ulcers subjected to vagotomy with gastroenterostomy.

One or more postoperative complications occurred in 37.7% of the patients after partial gastrectomy and in 25.8% of the patients after vagotomy with gastroenterostomy.

The postoperative mortality after partial gastrectomy was 4.9% as compared with 1.1% after vagotomy with gastroenterostomy. When the principal indication for surgery was pain, the postoperative mortality was 0.9% after partial gastrectomy and 1.1% after vagotomy with gastroenterostomy.

The commonest cause of death after partial gastrectomy was duodenal stump leak (7 of 17 cases).

Recurrent ulceration proved at surgery and/or by roentgenograms was noted in 2.2% of 231 patients followed after partial gastrectomy and in 7.6% of 131 patients followed after vagotomy with gastroenterostomy. Presumptive recurrent ulceration (hematemesis and/or characteristic ulcer pain) was noted in 1.7% of patients studied after partial gastrectomy and in 5.3% of patients studied after vagotomy with gastroenterostomy.

No significant difference was noted in the percentage of patients below average healthy weight after partial gastrectomy *vs.* vagotomy with gastroenterostomy.

No significant difference was noted in the incidence of the dumping syndrome after partial gastrectomy *vs.* vagotomy with gastroenterostomy.

Of surviving patients, 92.6% followed after partial gastrectomy and 84.0% followed after vagotomy with gastroenterostomy were satisfied with the operative result. However, when those patients who died after the operation were included among dissatisfied patients, patient satisfaction was 86.3% after partial gastrectomy as compared with 82.7% after vagotomy with gastroenterostomy.

840 S. Wood St.

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Arterial Homografts in Immediate Treatment of Severe Injuries to a Major Artery

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Since the first successful end-to-end anastomosis of a severed femoral vessel by Murphy 56 years ago, tremendous progress has been made in the surgical treatment of vascular diseases. None were more important or dramatic than the advances made in the successful repair of acute arterial injuries during the Korean conflict.[1] Thus, prior to 1952, injuries to major arteries were treated almost routinely by ligation. Even when primary anastomoses were attempted, results were seldom successful. An incidence of amputation due to gangrene of 62% was reduced following the institution of a successful program of arterial repair to 7%.[2] Although the proportion of civilian injuries due to penetrating wounds is smaller than in war casualties, the annual number of civilian accidents is increasing and necessarily entails many types of vascular injuries by a large number of persons. The National Safety Council recently reported approximately ten million civilian accidents a year, a majority of which involved the extremities. An understanding of the technique of treating arterial injuries during the emergency treatment is therefore necessary for all physicians who may be called upon in such acute emergencies. The following case represents such a vascular injury entering a large metropolitan hospital. Because of the availability of an arterial homograft and previous experiences in the treatment of vascular injuries, gangrene and amputation were avoided.

Report of a Case

A 39-year-old man was admitted to the surgical service on March 25, 1956, stating that he was accidentally shot in the left arm with a double barrel shot gun, two and one-half hours prior to admission.

Physical examination revealed a well-developed, well-nourished man complaining of severe pain in the left arm. Blood pressure was 122/80, pulse 80, and respirations 22. There were a few puncture wounds of the left anterior chest wall but many in the left upper arm. The arm was quite swollen. No pulse could be palpated in the anticubital fossa or at the wrist. The forearm and hand were cyanotic and cool. The neurological defect was difficult to determine, but there was evidence of damage to the ulnar, median, and radial nerves.

X-ray of the chest was negative except for several metallic foreign bodies in the skin and in the soft tissue of the arm. There was no evidence of fracture. Laboratory findings on admission were normal.

Patient was given I.V. fluids, antibiotics, tetanus and perfringens antitoxins. Because of the precarious condition of the forearm and hand, it was felt that exploration of the artery was indicated. This was carried out eight hours after injury. With the use of general anesthesia an incision was made over the medial aspect of the left arm. The tissues were edematous and blood-stained. A large clot was evacuated from around the vessels. The nerves were intact but contused in several places. There were multiple perforations of the brachial artery, beginning below the level of the profunda and extending down to about 2 in. above its bifurcation. The accompanying vein was perforated at several levels and was eventually ligated and removed. A 5 in. segment of brachial artery was removed and replaced by a homograft of femoral artery using end-to-end anastomosis with 00000 nonabsorbable surgical (silk) sutures. After the repair, the graft pulsated normally and the radial pulse could be easily palpated. Cyanosis and coldness disappeared. A relaxing incision was then made over the lateral aspect of the arm and the medial wound could be closed without tension. The open wound left by the relaxing incision was covered with a split thickness skin graft.

The patient did quite well after the operation. The radial artery was easily palpable at all times and the hand and forearm remained warm. Two months after the injury the patient had an arteriogram which showed patency of the graft (Fig. 1). Up to the time of discharge, motion was gradually returning in the arm. At present, the patient wears a radial nerve splint and is receiving physical therapy.

[Follow-up on the case reveals that the artery graft is functioning well as of March 1, 1957.]

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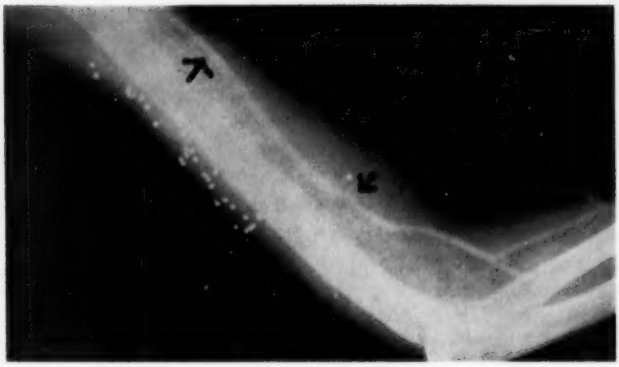

Arrows indicate extent of graft.

Conclusion

This case report is an example showing the value of a readily available artery bank and previous experience in the treatment of severe arterial injuries in a civilian general hospital. The successful application of this material and knowledge undoubtedly prevented gangrene and amputation in a person who had a retrievable injury to a large segment of the brachial artery.

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Limitations to Knitted Synthetic Tubes as Vascular Prostheses

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Since the report by Voorhees and associates in 1952 of the use of a weave of Vinyon-N as an artery substitute [7] several materials have been used with good results. One of the common disadvantages is the lack of elasticity. To overcome this, Sanger and associates [5,6] advocated knitting the grafts and have reported good results with knitted tubes of Orlon. The equivocal results obtained in this laboratory with knitted Orlon tubes replacing segments of the thoracic and abdominal aortas in 24 dogs have prompted this report.

Materials

Knitted Orlon tubes * of three types were used. The abdominal aortic grafts were of two types. One was knitted with 48 stitches per inch of a 200 denier Orlon (Fig. 1*A*) and had an air porosity † of 250. The other was knitted with 56 stitches per inch of a 200 denier Orlon and had an air porosity of 76 (Fig. 2).

The thoracic grafts were knitted with 48 stitches per inch of Type 42 Orlon fiber, a soft spun yarn possessing a high residual shrinkage and a fuzzy surface. These were placed on a tapered mandrel, heated, and shrunk. The inner surface was then singed. The resulting tube had thicker, more rigid walls and a lower porosity than the abdominal grafts (Fig. 1*B*).

Methods

Adult mongrel dogs were used in the study. Intravenously administered sodium pentobarbital was used for anesthesia. Endotracheal tubes were inserted, and oxygen was given by intermittent positive pressure with a pneophore valve. All arterial anastomoses were performed in the same manner with a continued over-and-over suture of 00000 artery nonabsorbable surgical suture after everting mattress sutures were placed at two corners.

Nine grafts were inserted into the thoracic aorta. The chest was entered through the fifth

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* Supplied through the courtesy of Prof. W. E. Shinn, North Carolina State College, Raleigh, N. C.

† Air porosity is the number of cubic feet of air that will pass through a square foot of fabric in one minute at an air pressure of 0.5 in. of water.

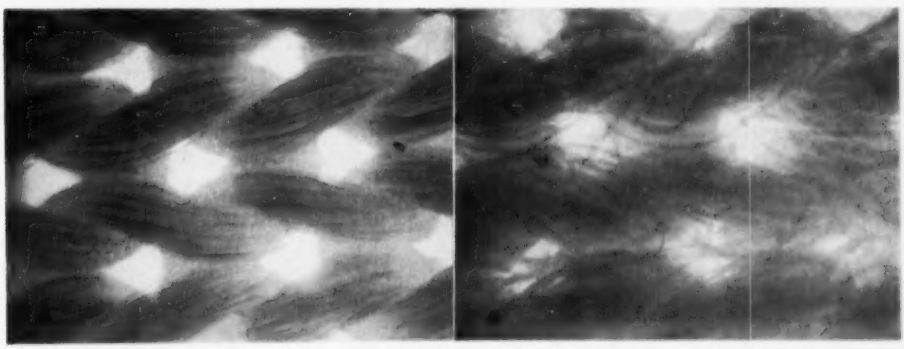

Fig. 1.—Photomicrographs of knitted Orlon grafts. *A*, abdominal graft, 48 stitches per inch. *B*, thoracic graft, 48 stitches per inch of Type 42 Orlon; note the rougher finish and smaller openings than in *A*. × 75.

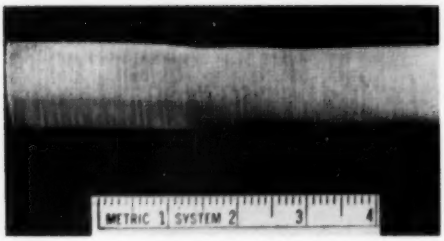

Fig. 4.—Knitted Orlon abdominal graft (56 stitches per inch).

intercostal space, and the aorta exposed from the arch distally 6 in. Six pairs of intercostals were ligated and divided. A shunt made of polyethylene tubing was placed between the left subclavian artery and the descending aorta during the period of occlusion. A segment of artery, 5 cm. in length, was excised between Pott's clamps and replaced by a tapered graft, the same diameter and 6 to 7 cm. in length. The shunt was then removed, and the defect in the aorta closed. The distal clamp was released, and blood allowed to fill the graft. After all bleeding had stopped, the proximal clamp was gradually released. The subclavian stump was ligated.

Fifteen grafts were inserted into the abdominal aorta. The abdomen was opened through a midline incision, and the aorta freed from the renal arteries to the trifurcation. A segment of artery, 4 to 5 cm. in length, was excised and replaced by a graft, the same diameter and 5 to 6 cm. in length.

Postoperatively, the dogs were given penicillin for one week. They followed carefully for changes in pulses, then killed at intervals up to six months. At the time of killing the animals were anesthetized and, while they were still alive, the grafts were visualized to evaluate the blood flow. All grafts were excised and studied grossly and histologically.

Results

Thoracic Aorta.—The polyethylene shunts functioned satisfactorily during the period of occlusion of the thoracic aorta; no animals developed shock or paralysis. All nine grafts remained patent during the six-month period of observation. Most of these animals have not been killed and are to be followed for longer periods.

Abdominal Aorta.—There were complications in 13 of the 15 grafts inserted into the abdominal aorta. Four became occluded by thrombosis during the 1st to 28th postoperative days. Bleeding through the interstices of the graft at the time of insertion was excessive but stopped after two to four minutes. During the early postoperative period there was a recurrence of the bleeding in nine of the animals, causing hematomas around the grafts. Associated with the hematomas were an abscess in one dog and thrombosis in one. There was delayed bleeding through the interstices of one of the three more closely knitted tubes (Table).

The uncomplicated grafts became enclosed in fibrous tissue capsules that were adherent by one month. Early a layer of fibrin was deposited on the inner surface that increased in thickness for three to four weeks. This was gradually replaced by

Results with Knitted Orlon Prostheses Replacing Segments of the Abdominal Aorta

Dog, No.	Length of Graft, Cm.	Diameter, Mm.	Follow-Up Period, Days	Cause of Death	Patent	Comment
426	6	8	½	Asphyxia from aspiration	+	Thin fibrin lining
283	6	8	1	Sac	0	Thrombosed
468	5	8	2	Paralysis	0	Thrombosed first 24 hr.
428	6	8	14	Peritonitis	+	Large hematoma and abscess
483	5	8	19	Ureteral obstruction from pressure of hematoma	+	Large hematoma
487	6	8	20	Sac	+	Hematoma
470	5	8	24	Sac	0	Large hematoma, thick fibrin lining, and thrombus
486	5	8	28	Sac	+	Hematoma
448	6	8	39	Sac	0	Thick fibrin lining and thrombosis at 28 days
477	6	8	61	Sac	+	Hematoma
447	6	8	145	Sac	+	Resolving hematoma
413	5	8	152	Sac	+	Resolving hematoma
572*	5	8	1	Sac	0	Thrombosed
573*	5	8	57	Sac	+	2 mm. fibrin lining
585*	5	8	90	Sac	+	Resolving hematoma

* Less porous grafts, 56 stitches per inch.

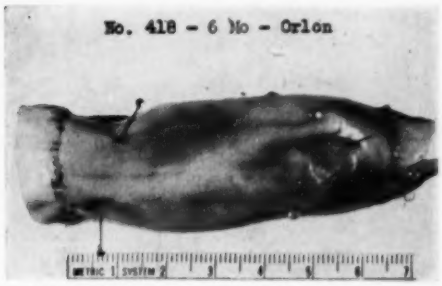

Fig. 3.—Dog 418. Knitted Orlon graft, thoracic aorta, 180 days. Note the smooth, glistening inner lining of the healed graft. Arrow points to bare area which was not healed owing to small hematoma surrounding this portion of graft.

fibrous tissue growing through the interstices of the graft. The healed grafts had smooth, glistening inner surfaces, grossly not unlike the intima of the host aorta (Fig. 3). They were enclosed in less dense fibrous tissue and were more pliable than nylon grafts followed the same period of time. The walls of the grafts did not pulsate at the time of insertion or at the time of killing.

Hematomas surrounding the abdominal grafts, caused by the delayed bleeding, interfered markedly with the healing process. The fibrin lining the inner surface was thick and ragged, and there were multiple bare areas where portions had become detached (Figs. 4 and 5). This was not replaced by fibrous tissue until the hematomas had resolved, and ingrowth could occur through the interstices of the grafts (Fig. 6). It is doubtful that the larger hematomas would have resolved. The scar tissue replacement of the hematomas caused a thicker fibrous enclosure of the grafts that did heal (Fig. 6).

Comment

The early results with the preshrunk knitted tubes of Orlon replacing the thoracic aorta were satisfactory. However, this is not too significant when evaluating grafts this size in that, of a total of 84 grafts of a variety of materials replacing the thoracic aorta of dogs in this laboratory, there has been occlusion in only one.[4] Delayed bleeding through the interstices cannot be completely excluded, since most of the animals have not been killed. The good healing in the ones observed indicates that, if there was bleeding, it was minimal.

The reported advantage of elasticity in the walls of the knitted grafts was not observed in this series either at the time of insertion or after healing occurred. The rigidity of the walls of a knitted Orlon tube, shrunk sufficiently to prevent bleeding, is such that significant elasticity will be present only at a pressure level above that in the major blood vessels.

The knitted tubes of Orlon used for replacing the abdominal aorta were too porous. It is felt that the delayed bleeding

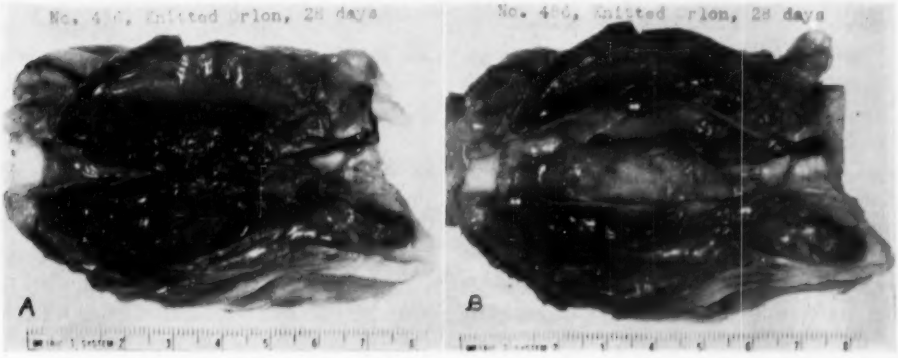

Fig. 4.—Dog 486. Knitted Orlon graft, abdominal aorta, 28 days. *A*, note large encapsulated hematoma surrounding the graft. *B*, opened graft; note the loosely attached fibrin and thrombi; healing has progressed across both suture lines.

Fig. 5.—Dog 483. Knitted Orlon graft, abdominal aorta, 28 days. Encapsulated hematoma surrounds graft, and thick layer of fibrin lining inner surface almost occludes the lumen.

Fig. 6.—Dog 447. Knitted Orlon graft, abdominal aorta, 145 days. Healing progresses as the hematoma is replaced by fibrous tissue. Note the thick fibrous enclosure of the healed portion.

with these was definitely through the interstices. Hematomas, resulting from bleeding through the suture lines or other points, have been observed infrequently in 250 grafts of other synthetic materials with an air porosity below 35, inserted by the same surgeon using the same technique.[4]

Bleeding through the interstices at the time of insertion can be controlled by blood replacement and experience with the technique of insertion of synthetic prostheses. Delayed bleeding, however, is uncontrollable and varies in severity from exsanguination to a hematoma around the graft. The hematoma, in addition to its usual complication, will cause a graft to have a thick, ragged, loosely attached fibrin lining until it undergoes resolution. In small grafts this will produce a high rate of occlusion. In large grafts, though occlusion is not likely, portions might become detached as peripheral emboli.

The tubes used for replacing the abdominal aorta were knitted as closely as possible with an Orlon yarn. The porosity can be reduced by shrinking the grafts on a mandrel at elevated temperatures, as was done with the thoracic grafts. This is accompanied by an increase in thickness and rigidity of the walls, which will cause a high rate of thrombosis from buckling, as the grafts will function more independently of the intra-arterial pressure.

Knitted grafts, to be successful for the replacement of vessels less than 9 mm. in diameter, must be made from small fibers that can be knitted into tubes with an air porosity less than 50 and still have thin walls. Present evidence indicates that other methods of preparation of the tubes, such as weaving or braiding, are preferable.[2,4]

The high incidence of complications in the abdominal grafts and the short term follow-up of the thoracic grafts preclude a complete evaluation of the relative advantages of Orlon per se as a vascular prosthesis. The results, in a comparative study of more than 200 synthetic grafts, indicate that it is preferable to nylon but not as good as Teflon. It incites less tissue reaction than nylon but more than Teflon [1] and at six months loses 12.8% of its original strength, while nylon loses 80.1% and Teflon gains.[2,3]

Conclusions

The results in this study indicate the limitations of knitted tubes as vascular prostheses. Orlon grafts knitted as closely as possible are too porous. Reduction of the porosity by shrinkage on a mandrel at elevated temperatures to a level that will prevent bleeding is accompanied by an increase in thickness and rigidity of the walls of the graft. Such prostheses are satisfactory for the replacement of segments of large vessels, but functional elasticity should not be expected. They are unsatisfactory for replacing vessels less than 9 mm. in diameter, as the thickness and rigidity of

the walls will cause a high rate of occlusion.

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Addendum

In animals killed after one year a loss of the tapering of the grafts in the thoracic aorta was revealed. There was an increase in the diameter throughout, resulting in a fusiform dilalation. The grafts had apparently returned to their original form that existed prior to heat shrinkage. This caused no trouble during the one year period, though any elasticity that might have resulted from the knitting would have been lost. The dilatation is felt significant as it might well occur with grafts that are woven by other processes to afford elasticity in the walls.

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Bilateral Rupture of the Quadriceps Tendon

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Bilateral rupture of the quadriceps tendon is a unique and uncommon injury. This is a report of such a case successfully treated. The treatment prescribed was surgical correction of the ruptured tendons. It is the opinion of the authors that with surgery complete rehabilitation of the knee is obtained with little or no morbidity.

Report of a Case

A 67-year-old white real estate dealer entered the hospital in June, 1956, because of inability to walk. He had been carrying a grill down the back stairs of his second-floor apartment and caught his right foot on a stair. He threw out his left leg but felt something give way, and his leg buckled from under him. He fell down to the next landing. He managed to get up, even though his left knee was painful and unstable. He again proceeded down the stairs. As he did, he felt pain and a "tearing" sensation in his right knee. He fell down the remaining stairs and was unable to get up. His neighbors helped him to his feet, but he could not walk or support his weight.

Previous health had been good. Past history was not significant. A traumatic perforation of the right eye at 8 years of age left total blindness in that eye. The patient was normotensive and had a regular pulse. His heart, lungs, and abdomen revealed no abnormalities. The external surfaces of both knees were contused, and a marked joint effusion was noted. Extension of both knees was completely lost. With the legs held straight, flexion at the knee was normal.

A diagnosis of bilateral rupture of the quadriceps tendon was made. Roentgenograms of the knees revealed no fracture. Hemogram and urinalysis were normal.

Immediate surgery was recommended. With the patient under general anesthesia, exploration of both knees was undertaken. The right knee was opened through a 6 in. midline vertical incision. The quadriceps tendon was severely contused and completely severed just superior to its patellar insertion. There was an extensive laceration of the joint capsule and marked hemarthrosis. The patella was intact. The edges of the quadriceps were débrided, and the wound irrigated with isotonic saline. Muscle continuity was restored with black nonabsorbable surgical interrupted mattress sutures. A flap of infrapatellar fascia was dissected free, and the distal end brought up and tacked over the initial anastomosis. A stainless-steel Bunnell-type "pull-out" wire was inserted through the quadriceps tendon and brought out through the skin anterior and inferior to the knee joint. This was used to eliminate tension on the suture line. The capsule of the knee joint and the skin were closed with interrupted black nonabsorbable surgical sutures. The pathologic findings and the anatomic surgical repair were the same on the left side. Both knees were immobilized in cylinder casts.

The clinical course was uneventful until the 12th postoperative day when a pneumonitis developed. An appropriate antibiotic was prescribed, and resolution occurred one week later.

Skin sutures and pull-out wires were removed on the 21st postoperative day. Cylinder casts were reapplied for three more weeks. After six weeks of immobilization, physical therapy was begun. Heat and message were given daily for one week. During this time the patient was encouraged actively to flex and extend his knees. At the end of the second week, he had relearned to walk with the aid of parallel bars. Cooperation was excellent, and eight weeks after surgery he was walking with aid of a cane. He returned to his business and has continued to improve.

Fig. 1.—Flexion of knees 10 weeks after surgery.

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Resident Surgeon, Cook County Hospital (Dr. Hinkamp), and Chief, Orthopedic Service, Illinois Central Hospital (Dr. Pellicore).

Fig. 2.—Extension of knees 10 weeks after surgery.

Fig. 3.—Full weight-bearing 10 weeks after surgery.

Comment

Bilateral rupture of the quadriceps tendon is not a common entity. The English and American literature reports only 10 cases. In one of these, there was a six-year interval between rupture of the respective tendons.

The anatomic arrangement of the quadriceps extension mechanism does not make it susceptible to rupture. Anatomically this extension mechanism has a suprapatellar and an infrapatellar segment. The suprapatellar portion is composed of three layers: an anterior layer containing the rectus femoris tendon; a middle layer comprised of the vastus lateralis and medialis tendon, and a deep layer composed of the vastus intermedius. All four tendons insert into the base of the patella. The inferior segment is the infrapatellar ligament. This begins at the apex of the patella and inserts into the tibial tuberosity. It is a continuation of the rectus femoris tendon. This ligament fixes the patella to the tibia.

Tendon expansions from the distal portions of the medial and lateral vasti muscles pass over the anterior surface of the patella and fuse with the fascia of the thigh. In this manner the patella is held immovable, and the capsule of the knee is strengthened. Strong fibrous bands connect the patellar margins to the tibial plateau and tibial condyles. These add to the stability of the knee.

The etiology of this condition is obscure. It is known that normal muscle and tendon do not rupture even when submitted to severe strain. Conway [12] has quoted McMasters' experimental studies in animals to support this. McMasters also found that if a tendon segment was deprived of its blood supply it became susceptible to rupture when severe strain was applied. Aging, with its loss of tissue elasticity, metabolic diseases and degenerative diseases of the muscles and joints are predisposing causes. A violent contracture of the quadriceps with the knee and foot flexed is the immediate cause of the tear.

The diagnosis is usually not difficult. There is a history of trauma followed by pain and effusion in the knee joint. Extension of the knee is not possible. There is usually hypermobility of the patella. A depression may be palpable where the tendon has been separated. Roentgenograms reveal an intact patella.

With surgical treatment the prognosis is favorable. Surgical correction has been the treatment of choice since McBurney [11] reported the first successful repair of a quadriceps tendon laceration in America in 1887. McBurney approximated the tendon edges with quill sutures. He then secured his sutures by passing silver wire through the edge of the patella. Since McBurney's time many techniques using absorbable and nonabsorbable surgical sutures, wire, kangaroo tendon, and fascia lata strips have been used to restore muscle continuity. Two of the earlier cases [2,3] healed without surgery, but the morbidity was prolonged.

The exact type of repair depends on the pathology found at operation and the ingenuity of the surgeon. In essence the tendon anastomosis must be effected without tension. Because of the longitudinal arrangement of the tendon fibers, there is a tendency for simple sutures to tear away. In our case the Bunnell-type, pull-out wire was used to eliminate any pull on the suture line.

In this case six weeks' immobilization proved adequate for healing. A week of heat, massage, and active quadriceps exercises helped rehabilitate the knees. The second week the patient relearned to use his legs with the aid of parallel walking bars.

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Effect of Hepatic Arterial Ligation on Hepatic Blood Flow and Related Metabolic Function

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The presence of collateral arterial circulation to the liver has been deemed essential to the survival of animals subjected to hepatic arterial ligation. Such channels to the liver have been reported to originate from the diaphragm and pancreaticoduodenal area as well as through small arteries coursing along the inferior vena cava and common bile duct. Tanturi [1] has stated that these channels cannot provide enough blood to account for the animal's survival and has occasionally found animals without collateral circulation. Markowitz [2] has commented that there is nothing about the anatomy of the liver which makes the hepatic artery essential to an animal's survival.

This study was undertaken in an attempt to determine the pattern of development of collateral arterial circulation and to study hepatic blood flow and related metabolic functions in animals whose liver has been deprived of its highly oxygenated blood supply.

Methods

The hepatic arterial supply to the liver was removed surgically in 27 animals. The abdomen was opened aseptically with a midline incision. The main hepatic artery was located and isolated from its surrounding sheath approximately 1 in. above its departure from the celiac artery. A small branch leading to the right lobe of the liver was generally located in this area and was ligated and sectioned. At this point the cleared portion of the hepatic artery was passed under the portal vein to facilitate further clearing and provide access to the remaining connections between the hepatic artery and liver proper. All other branches to the liver were located at their entrance to this organ and ligated and sectioned, leaving intact the free loop of vessel consisting of the common hepatic artery and the gastroduodenal artery. If the right gastric artery arose from the hepatic artery proper, it was also ligated and sectioned. The number of these hepatic branches varied from two to seven. Upon completion of the surgery the hepatic artery was returned to its original position and the incision was closed. Penicillin therapy [3] was administered three days prior to and four days following the operative procedure in 21 animals. Surgery was performed on six animals without the benefit of antibiotic treatment.

After a time lapse adequate for recovery from the operative procedure, the estimated splanchnic blood flow and splanchnic oxygen consumption were determined on each surviving animal. Forty-one experiments were done on 15 dogs. The animals were anesthetized with sodium pentobarbital (30 mg/kg. body weight) and heparinized (5 mg/kg. body weight). Under fluoroscopic visualization a single-lumen cardiac catheter with a three-hole tip was inserted into an exposed jugular vein and guided into a main hepatic vein. A branch of a femoral artery and a cephalic vein were cannulated for sampling and infusion purposes, respectively. Estimated splanchnic blood flow was determined by the method described by Bradley et al.[4] and modified by Werner and Horvath.[5] Blood samples were drawn from the femoral artery and hepatic vein for analysis of their oxygen content by the method of Van Slyke and Neil.[6] Oxygen consumption was determined with a Benedict-Roth metabolism apparatus, and hematocrits were measured by the Wintrobe tube technique. Blood pressures were recorded from the femoral artery and hepatic vein by means of Statham pressure transducers and appropriate amplifying and recording equipment. The point of zero reference for the blood pressures was the right atrium. Upon termination of the experiment the animals were given 300,000 units of

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penicillin, intramuscularly, and returned to their cages.

Following the final experiment on each animal, the animal was killed and autopsied. A liver injection technique (plastic plus radio-opaque coloring material) was employed to evaluate the success of the operative procedure and locate any collateral circulation that may have developed. The aorta was clamped above the diaphragm and below the origin of the celiac artery. Another clamp was placed on the aorta in the region of the arch and an injection of a plastic of another color was made into the aorta distal to this clamp. X-ray photographs were made of these injection specimens and the liver cast was preserved by digesting the tissue and leaving the circulatory system intact. Histological sections were made of the livers for microscopic examination.

All results were statistically analysed using the unpaired *t* test, and the null hypothesis was rejected at the 5% level of significance.

Results

Hepatic arterial ligation was performed on a total of 27 animals. Fifteen of the twenty-one animals receiving penicillin pre- and postoperatively, survived the surgical procedure and the remainder died within three days. All these later animals exhibited massive liver necrosis. None of the animals not receiving antibiotic therapy survived the operative procedure.

The animals surviving the procedure were maintained at the laboratory for periods of time varying from 47 to 534 days postoperatively. No arterial blood supply from the hepatic artery to the liver was found in any animal nor was any collateral circulation located.* A study of histological sections of the livers was made and no evidence of arterial circulation could be found in those animals surviving the surgery.

Experimental studies of estimated splanchnic blood flow and related functions were conducted on these animals at various times following the surgery. A comparison of this data with that collected from animals with their arterial circulation intact is presented in the Table. The animals operated upon were divided into four groups on the basis of the days after surgery on which the experiments were made. Experiments were performed on the 15th, 57th, 250th, and 433d day after the hepatic artery was ligated. The hepatic blood flow was not significantly different from control following ligation at any of the time intervals measured. Although there appears to be a slight decrease in the mean values with the increasing period without an arterial supply, the inherent variability precluded any statistically significant change.

The extraction of sulfobromophthalein sodium (Bromsulphalein; BSP) was not altered by the hepatic arterial ligation two weeks after surgery. However, the extraction at 57 days was significantly higher than at both 15 days and control values. The BSP extraction did not deviate from control at any other time.

The splanchnic oxygen consumption was not altered at any time. Although the 15-day reading was higher than control (36.0 as compared with 28.2), the difference was not statistically significant. The per cent of the total oxygen consumption used by the splanchnic bed was changed from control only at 250 days after surgery. This value of 26.7% at 250 days postoperatively was significantly lower than control at the 5% level and from the 15 and 57-day readings at the 1% level. However, after 433 days the per cent oxygen used by the splanchnic bed was similar to the control values. Therefore, the oxygen consumption per cent showed a general trend of a rise immediately following surgery which persisted for 57 days and a sharp fall at 250 days followed by a return to control at 433 days. These values are a reflection of an increased total oxygen consumption at 250 and 433 days. Splanchnic vascular resistance did not change, remaining at an absolute value of 0.20 units throughout the study.

The arterial oxygen content showed a significant decrease after surgery. This in-

* On the basis of work in progress there is some evidence that in certain circumstances a collateral channel arising from a branch of the phrenic artery can be observed. However, this appears to provide only a very minor amount of arterial blood to the liver. Much of this arterial supply appears to enter the liver by following along the hepatic veins.

Hepatic Metabolism in Normal Animals and in Animals Without Hepatic Arterial Supply

Number of Observations	Controls, Not Operated on 49		Hepatic Arterial Ligation							
			Days After Surgery 15 7		57 15		250 10		433 9	
	Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.
Arterial O_2, vol.%.....	19.1	0.36	16.7	0.81	17.4	0.79	17.5	0.71	18.6	0.96
Arterial hepatic vein O_2 Diff. Vol.%.....	5.04	0.44	5.42	0.60	5.02	0.39	4.98	0.46	4.77	0.70
Splanchic blood flow, ml./min..	649	25	648	83	623	43	590	69	591	99
Total O_2 consumption, ml./min.....	87	3.0	93	9.2	84	6.1	104	6.8	106	7.5
Splanchnic O_2 consumption, ml./min.....	28.2	2.0	36.0	4.8	30.0	2.3	29.2	3.6	33.9	7.4
Per cent of total O_2 Consumption used by splanchnic bed	32.8	2.0	37.5	2.9	36.8	2.8	26.7	2.0	32.4	6.6
Splanchnic vascular resistance units.....	0.20	0.01	0.19	0.04	0.20	0.03	0.24	0.02	0.20	0.03
BSP extraction, %.....	40.5	1.6	36.0	4.1	48.2	3.2	37.1	5.6	44.0	6.4
Heart rate, beats/min.....	143	3.4	135	9.4	146	8.9	167	11.8	156	14.5
Mean femoral arterial blood pressure, mm. Hg	130	2.6	119	7.7	132	30.4	130	9.6	145	12.0
Mean hepatic vein blood pressure, mm. Hg.....	2.3	0.6	2.6	1.2	3.5	0.7	2.6	0.5	2.0	0.4

itial fall was marked, 19.1 vol. % to 16.7 vol. %, and could indicate that surgical recovery was not complete at this time. Later values were significantly below control (0.5% level) at 57 days and 250 days and within control range at 433 days. Arteriohepatic vein oxygen differences were not influenced by the hepatic arterial ligation. There was no significant change in either arterial or hepatic venous pressures as a consequence of the ligation.

Comment

It has been demonstrated that penicillin administered pre- and postoperatively greatly increases the percentage of animals sur-

Fig. 1A.—X-ray photograph of the arterial circulatory supply to the liver in the normal dog following injection of the aorta with radio-opaque dye solution.

Fig. 1B.—X-ray photograph of the liver from an animal 475 days following removal of the arterial blood supply to the liver. The aorta was injected with a radio-opaque dye solution.

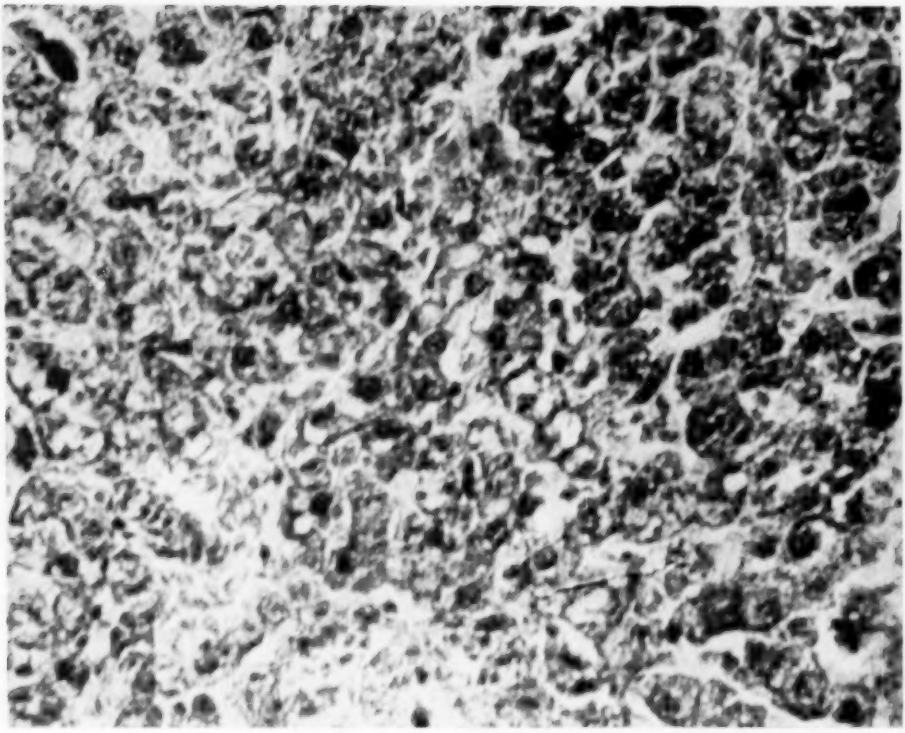

Fig. 2A.—Section of the liver from an animal with an intact arterial blood supply to the liver.

viving hepatic arterial ligation.[1-3] All animals which did not receive antibiotic treatment died one to two days after surgery. However, 6 of the 21 animals which had penicillin treatment also died after the operation. Grindlay[7] reported a 50% survival in animals receiving penicillin and stated that the recovery appeared to be related to the development of an adequate number of vessels supplying the hepatic arterial circuit. In this series of animals the collateral circulation was minimal; if it existed at all, it was not of sufficient quantity to appreciably alter the oxygen supply to the liver. Figure 1 is an x-ray photograph of an injected normal liver and also of a liver injected 475 days after removal of its arterial blood supply. Injection was made into the aorta above the diaphragm following clamping of the aorta at the arch and below the origin of the celiac artery. The lack of arterial circulation can be observed by comparing the dog operated upon with the normal animal. Thus, the extent of development of collateral circulation did not appear to be the underlying factor in the survival of these animals. Since Bollman et al.[8] have reported no change in splanchnic blood flow in hepatic arterially ligated animals just two days after surgery, it would appear that the portal venous flow was able to compensate for the loss of the major arterial supply very rapidly. In the present series the splanchnic blood flow was the same in control and experimental animals from two weeks to more than a year after ligation.

The BSP extraction, one index of liver function, remained within normal range throughout the series of observations. Therefore, it would appear that the liver tissue itself was not seriously damaged by

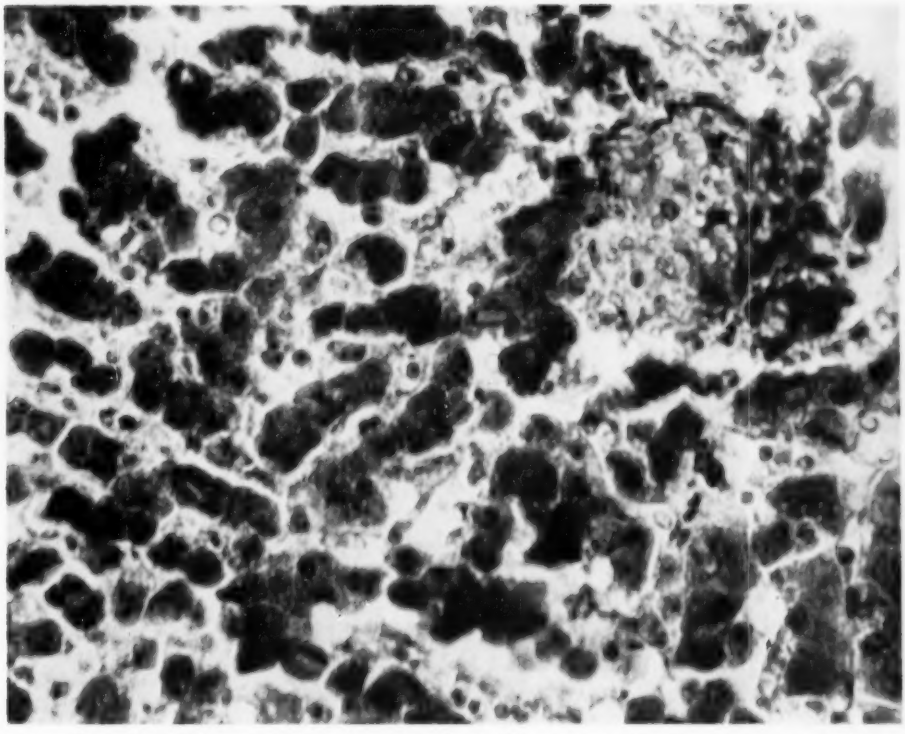

Fig. 2B.—Section of the liver from an animal 475 days following removal of the arterial circulatory supply to the liver.

the loss of a large amount of its highly oxygenated blood. There was no evidence of liver necrosis in those animals which recovered from the operation and were sacrificed at a later date. Some changes were observed upon microscopic examination of the liver tissue. Histological sections of normal liver tissue and of liver taken from an animal 475 days following hepatic arterial ligation showed (Fig. 2) marked atrophy and dissociation of liver cells in the venous liver animal. Similar changes occur in hypoxic livers, but the degree of ischemia observed in these animals was insufficient to induce necrosis. Since a constant splanchnic oxygen consumption was observed both before and at the specified times after surgery, the animals were probably not hypoxic to any great extent.

It would appear from the data presented that the portal venous inflow is adequate to maintain the liver tissue from the standpoint of supplying sufficient oxygen to prevent serious liver cell damage. Whether this situation would persist unchanged, if the venous liver animal were maintained for longer periods of time cannot be answered at this time but provocative evidence exists from the histological pictures of the livers that eventual damage could occur.

Summary

No change in hepatic blood flow and associated metabolic functions was observed in animals at any time up to 534 days following complete hepatic arterial ligation. It would appear that the portal venous blood supply is sufficient to maintain the liver tissue. Some minor histological changes

were observed in the livers of animals after interference with the arterial circulatory supply of the liver.

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The Significance of Diverticula of the Colon in Massive Melena

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Massive melena without hematemesis is often a challenging diagnostic problem. Diverticula of the colon demonstrated in such cases are often overlooked as the source of bleeding. Furthermore, both the clinician and the pathologist have been reluctant to accept diverticula as the source of hemorrhage because a bleeding point may be difficult to demonstrate, even at autopsy. To evaluate the frequency and magnitude of hemorrhage from these lesions, 317 unselected patients with diverticula of the colon were surveyed.

The incidence of diverticulosis of the colon has been estimated at 5 to 10% of all the population over 40 years of age. This has been substantiated by Sauer [1] who found them in 5.2% of 70,572 subjects examined, and by Pemberton, Black, and Maino [2] who found them in 8.5%. Rankin and Brown [3] have stated that 15 to 20% of all those with diverticulosis will develop diverticulitis. Therefore, it seems logical to assume that if diverticula cause hemorrhage from the colon, as many authors contend,[4-11] it should occur rather frequently. An incidence of up to 45% of gross hemorrhage in patients with diverticulitis has been reported.[11] Greater attention is justifiably being given this complication and its management.

The frequency with which diverticula of the colon occur in patients with severe melena, in whom no other etiologic lesion could be demonstrated, has been impressive. The records of 317 unselected patients discharged from this hospital with the diagnosis of diverticulosis or diverticulitis have been reviewed. Several patients who probably bled from diverticula were excluded because a coexistant gastrointestinal lesion that could have produced hemorrhage was demonstrated. Specific criteria should be fulfilled before melena is attributed to diverticula (Table 1): (1) bright red rectal bleeding without hematemesis; (2) demonstration of diverticula and exclusion of any other potentially bleeding lesion by barium enema, air contrast study, and sigmoidoscopy; (3) negative upper gastrointestinal series; (4) normal coagulability of blood. Furthermore, to exclude the possibility that another lesion such as peptic ulcer, tumor, or polyp was missed, the patients who had severe bleeding were followed from 4 to 10 years. Various authors reporting the incidence of hemorrhage from diverticula have not included follow-up studies.

TABLE 1.—*Were Diverticula the Source of Bleeding?* (*Nineteen Cases*)

1. 18 had negative upper G.I. series
2. Patients with any other G.I. lesion excluded
3. All had bright red bleeding
4. All had negative sigmoidoscopies
5. Two readmitted with bleeding; reevaluation negative for other lesions
6. Diverticula occur at points of entrance of end arteries into colon

Sixty (19%) of the 317 patients had either massive hemorrhage, gross bleeding, or stools repeatedly positive for occult blood by the guaiac test. Nineteen (6%) had massive hemorrhage and constitute the basis for the remaining presentation (Fig.). Their age range was 39 to 81 years, the average age, 69. Incidence by sex was about equal—10 females and 9 males. Over 60% were obese.

The presenting complaint in all 19 cases with massive hemorrhage was "rectal bleed-

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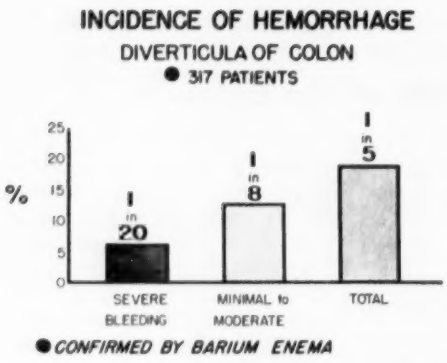

ing." Thirteen also had syncope or subjective symptoms of shock. Their past history was significant in that six had previous bleeding and six had experienced lower abdominal pain or tenderness.

An indication as to the severity of the hemorrhage is furnished by the following findings: (*a*) the admission hemoglobin was 9 gm. or below in 9 of the 19 patients; (*b*) it fell to 9 gm. or below sometime during the hospital course in 15; (*c*) the lowest recorded hemoglobin was 6 gm.; (*d*) the maximum amount of blood to replace the deficit was 6000 cc. in one patient; (*e*) the average volume of blood required from replacement in the entire group was 2100 cc. and (*f*) 14 patients (82%) required 1000 cc. or more of blood (Table 2).

The management was conservative in all cases and essentially consisted of adequate blood replacement and administration of usual dosage of one of the nonabsorbable sulfonamides or neomycin sulfate. The patients were discharged with instructions to continue the medication for one week each month.

The temptation toward surgical intervention during massive hemorrhage is often tempered by distribution of the diverticula over most of the colon and inability to demonstrate the specific site of bleeding. Therefore, total colectomy in such instances would be necessary to assure resection of the bleeding area. The advisability of such a procedure in a poor-risk patient for a benign lesion is questionable in light of the fact that all 19 patients in this series survived with conservative management. An occasional patient with rapid, persistent, massive bleeding, however, may require emergency resection. If the diverticula are limited to the left colon in such a patient, resection should be feasible; but if they are distributed over most of the colon, it might be prudent first to establish a transverse colostomy to localize the site of hemorrhage. Hemicolectomy instead of total colectomy would then be sufficient. These procedures have not been necessary in this series.

TABLE 2.—*Severity of Hemorrhage from Diverticula (Nineteen Cases)*

Hemoglobin
Admission values, 9 gm. or lower in 9 cases
During hospitalization, 9 gm. or lower in 15 cases
Lowest recorded—6 gm.
Blood required
Maximum replacement—6,000 cc.
Average replacement—2,100 cc.
14 required 1,000 cc. or more

The decision against resection in these cases can be based on these facts:

1. Diverticula were widely distributed over the colon in those with the severest hemorrhage.

2. Obesity and other factors increasing the hazard of surgery were common.

3. There was an insufficient interval for preparing the colon with nonabsorbable sulfonamides or neomycin sulfate.

4. The mortality is up to 50% in reported cases with resection.[8,11]

5. There were no deaths in this series.

Follow-up of these 19 cases over an interval of 4 to 10 years has shown that 10 are surviving. Of these ten, eight have had no recurrent hemorrhage and two have bled again but were reevaluated and no other lesion was demonstrated. Seven patients have died of unrelated disease 3 to 32 months after the initial hemorrhage but none had recurrence of bleeding. Two of the nineteen cases were lost to follow-up. No patient included in this survey has been known to die of hemorrhage (Table 3).

TABLE 3.—*Follow-Up Study of Nineteen Patients with Severe Hemorrhage*

2 Patients lost to follow-up	
17 cases followed	
10 patients surviving and followed 2 to 5 years	
8 patients—no recurrent hemorrhage	
2 patients—readmitted with recurrent hemorrhage; no other lesion demonstrated	
7 patients expired of unrelated disease 3 to 32 months after initial hemorrhage. None had recurrence of bleeding	

Comment

The probability of diverticula of the colon as the source of bleeding in a patient with severe rectal bleeding should not be minimized. Diverticulosis may prove to be second only to peptic ulcer as a cause of massive melena without hematemesis.[12] Severe bleeding occurred in 6% and some degree of bleeding in 19% of this series. This finding and similar experiences of others should furnish added impetus to the acceptance of elective resection in patients with complications of diverticulosis. However, the high mortality reported for emergency resection and survival of all conservatively managed patients in this series should raise serious doubt concerning the advisability of urgent surgical intervention in all but exceptional cases.

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Experimental Study of a Gradually Closing Delayed-Action Blood Vessel Clamp

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Numerous methods have been proposed for producing slow and gradual occlusion of blood vessels.[1-4] In previous communications[5-6] we have outlined the problems associated with some of these methods and proposed a new steel clamp for producing gradual occlusion. This clamp is applied around a blood vessel with the jaws held apart by a bolus of absorbable surgical suture. After contact with the body fluids the suture is slowly absorbed, and the jaws of the clamp occlude the vessel (Fig. 1).

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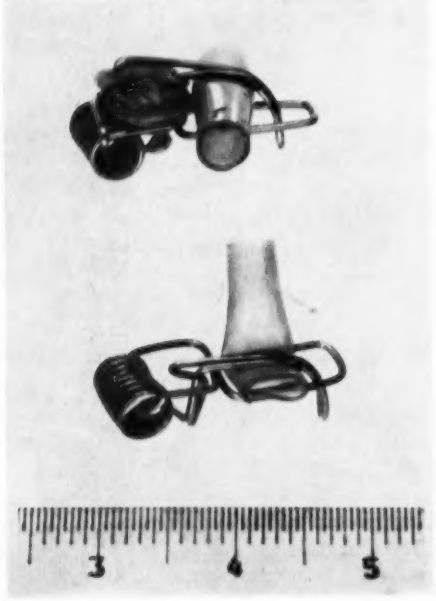
Fellow of the New York Heart Association, 1955-1956 (Dr. Lowenfels); Fellow of the New York Heart Association, 1954-1955 (Dr. Wade).

Fig. 1.—Photograph of self-closing blood vessel clamp. The upper picture shows how a bolus of absorbable surgical suture keeps the jaws of the clamp apart. The lower picture reveals how the jaws close around a simulated blood vessel after absorption of the suture. Scale is in centimeters.



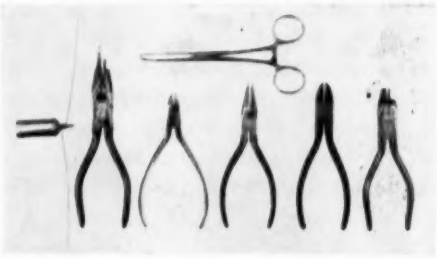


Fig. 2.—Mandril and tools used to construct spring-steel clamp.

Continued experience with this method of vascular occlusion has shown it to be a useful and simple experimental tool for the delayed action closure of many different blood vessels. Since exact information was lacking concerning the rate and manner of vascular occlusion as produced by this clamp, a new series of experiments was designed to clarify its action.

Materials and Methods

The clamp used is constructed of hard-tempered stainless-steel wire, SMO 18-8 Type 302, having a diameter of 0.064 cm. This type of steel has been shown to be nonreactive in body tissues. It is used to fashion an eight-coil spring by winding it around a mandril, 0.32 cm. in diameter. The ends of the spring thus formed are left protruding at right angles to each other, and the remainder of the clamp is fashioned with a set of specially designed tools (Fig. 2). Several stages in the construction of the clamp are shown in Figure 3. All clamps are tested to insure that they will withstand a pressure of 200 mm. of mercury in the closed position.

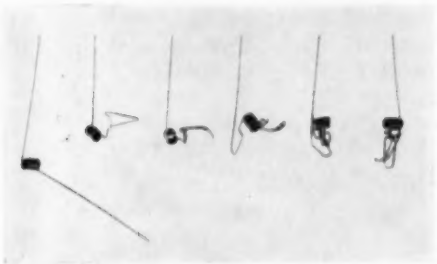


Fig. 3.—Several stages in the construction of the clamp.

In Vitro Study of Absorbable Surgical Suture Absorption.—Although ample information is available dealing with the absorption of absorbable surgical suture under tension, no data were found concerning the behavior of this suture when subjected to compression forces. Since the action of this clamp depends upon the absorption of the suture under compression, it was thought that preliminary in vitro studies of suture absorption would be useful.

The clamp, as described above, was wound with 50 turns of 00 plain or chromic nonboilable absorbable surgical suture and placed in a digestion bath consisting of 10% pepsin and 1% concentrated hydrochloric acid.[7] The digestion bath was maintained at 37 C, and the enzyme solution was changed daily. The clamps were allowed to close around a thin-walled rubber tube which was connected to a fluid reservoir. At half hourly or hourly intervals the rate of flow of water from the reservoir 100 cm. above the clamp was measured and then recorded photographically with use of an apparatus similar to that described by Tadayon.[8]

In Vivo Studies.—In a second series of experiments, the in vivo behavior of these clamps was studied by burying them in the tissues of dogs. Fifteen clamps were prepared with 50 turns of 00 plain absorbable surgical suture and then buried in the subcutaneous tissue of the interscapular region. The clamps were allowed to close on a thin-walled flexible rubber tube (0.32 cm. inside diameter) whose ends projected through the skin. The progress of closure was followed by pouring water through the tubes from a height of 100 cm. and recording the flow in cubic centimeters per minute.

In a similar fashion six clamps were buried within the pericardial sacs of dogs and studied in the same manner. Each of the clamps in this group was wound with 50 turns of 00 plain absorbable surgical suture.

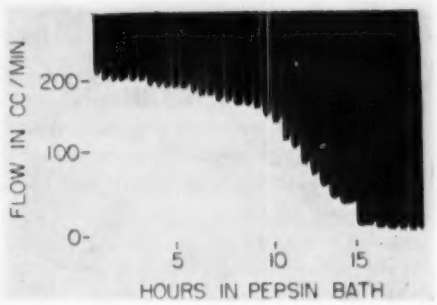


Fig. 4.—Photographic record showing changes in flow which occur when a clamp wound with 00 plain absorbable surgical suture closes around a thin-walled rubber tube in an acid-pepsin digestion bath.

Results

In Vitro Study.—With use of the in vitro method, as outlined above, the average closure time for 21 clamps wound with 00 plain absorbable suture was 14.4 hours (standard deviation, 4.9 hours). A typical curve obtained in this fashion is shown in Figure 4.

Chromic absorbable surgical suture was also studied, and the average closure time required for six clamps wound with 00 chromic nonboilable suture was 110 hours (standard deviation, 13 hours).

The changes in flow which were recorded when the clamps were wound with plain absorbable surgical suture were not linear. During the first two-thirds of the total time

Closure Times for Clamps Prepared with 00 Plain Absorbable Surgical Sutures and Implanted in Dogs

Location of Clamp	Last Day Observed Open	Day of Observed Closure
Subcutaneous tissue	21	28
Subcutaneous tissue	21	28
Subcutaneous tissue	21	28
Subcutaneous tissue	21	28
Subcutaneous tissue	21	28
Subcutaneous tissue	12	28
Subcutaneous tissue	12	28
Subcutaneous tissue	17	24
Subcutaneous tissue	10	17
Subcutaneous tissue	10	17
Subcutaneous tissue	10	17
Subcutaneous tissue	9	16
Subcutaneous tissue	9	16
Subcutaneous tissue	6	12
Subcutaneous tissue	6	12
Pericardial sac	13	22
Pericardial sac	15	16
Pericardial sac	12	15
Pericardial sac	12	13
Pericardial sac	7	10
Pericardial sac	8	9

required for closure, very little change in flow was noted. During the last one-third, the flow rapidly diminished to zero.

When chromic absorbable surgical suture was used, there was a considerable lag period before any change in flow was recorded. In some cases flow remained unchanged until the last 10 hours in the digestion bath.

In Vivo Studies.—The closure time for 21 clamps buried in the subcutaneous tissues and the pericardial sacs of dogs are recorded in the Table. Most of these clamps closed between two and three weeks after implantation. Earliest observed closure occurred on the 9th day, and others had not closed until the 28th day. A moderate inflammatory reaction developed in the tissues surrounding some of the clamps which were buried in the subcutaneous tissues.

The closure time for the six clamps implanted in the pericardial sac fell within the observed range for clamps buried in the subcutaneous tissues. Two of the animals, not listed above, died of empyema in the first week before closure was complete.

The manner in which these clamps closed was of particular interest. Almost all the clamps studied showed an initial increase in flow after implantation. This was followed by a lag period lasting up to one week, in which flow past the clamp remained essentially unchanged. During the remainder of time in which the clamp remained open, flow decreased to zero in a period of time requiring from three days to two weeks. A typical curve obtained from a clamp buried in the pericardial sac is shown in Figure 5.

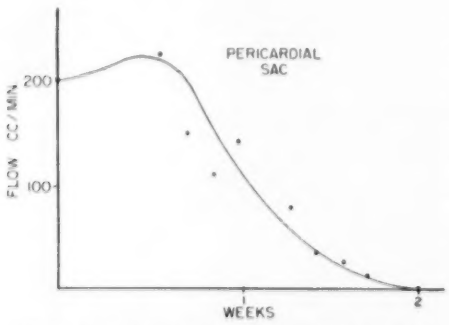


Fig. 5.—Graph showing flow changes which occur when a clamp wound with 00 plain absorbable surgical suture closes around a thin-walled rubber tube which has been placed in the pericardial sac.

Comment

When subjected to enzymatic action of an acid-pepsin solution, the absorbable surgical suture used to separate the jaws of this clamp softens, fragments, and then gradually disappears. That the effect of such gradual occlusion does not necessarily produce a corresponding gradual reduction in flow has been noted before by Mann and his co-workers.[9] Also, as pointed out by Shipley and Gregg,[10] the peripheral resistance mechanism distal to the constricting clamp plays a highly important role in determining the amount of reduction of flow through the vascular bed.

When the clamps were placed around thin-walled rubber tubes and allowed to close in the body tissues, rather characteristic flow curves were obtained. An initial period of increased flow can probably be correlated with swelling of the suture fibers prior to disintegration. This is followed by a period of closure usually complete in the second or third week after implantation. Of interest was the fact that the rate of closure appears to be the same for the pericardial sac as for the subcutaneous tissue.

These clamps have been used in a group of approximately 75 dogs to produce occlusion of the coronary, carotid, and renal arteries[11] and also of the portal vein. By using these clamps, one is able to occlude important areas of the vascular system without recourse to multiple-stage procedures. The period of gradual closure serves to stimulate collateral vessels and thus allow an organ to survive when deprived of its main nutrient supply. In this fashion dogs have been prepared with occlusion of major amounts of the coronary arterial supply.[12]

In some of the early clamps abrupt closure was an occasional problem. This does not seem to occur with the present clamp which has been modified to prevent slipping

of the suture when moistened by the tissue fluids.

When the present clamp is applied to a large artery, such as the aorta of the dog, continued pulsation of the vessel against the constricting jaws of the clamp has produced erosion with subsequent recanalization of the artery.

In a few instances, persistence of the suture within the jaws kept the clamp from closing fully. This was usually associated with the use of chromic absorbable surgical suture, but in one case a clamp wound with 00 plain absorbable surgical suture was found to be unchanged 18 months after implantation around the left coronary artery.

Summary

A stainless-steel spring-activated clamp whose jaws are separated by absorbable surgical suture and which is capable of producing gradual vascular occlusion has been developed.

Clamps wound with 00 plain absorbable surgical suture require an average of 14.4 hours to close in an acid-pepsin bath at 37 C as compared with clamps prepared with 00 chromic absorbable surgical suture which require an average of 110 hours for closure.

In vitro digestion studies suggest that absorption of the suture used between the jaws of this clamp proceeds in a gradual fashion. However, gradual external constriction causes relatively little diminution of flow until the later phases of closure are attained.

Clamps whose jaws have been separated with 00 plain absorbable surgical suture and which are buried in the subcutaneous tissue of dogs require from one to four weeks for complete closure. Clamps buried in the pericardial sac also close within this same time interval.

55 E. 92d St. (28) (Dr. Lord)

Mr. Sol Gelman rendered technical assistance in this experimental study. The hard-tempered stainless-steel wire used in constructing the clamp was supplied by the ABC Spring Company, 16 W. 22d St., New York. The absorbable surgical suture was supplied by Davis & Geck, Inc., Danbury, Conn.

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Some Clinical Observations in Problems of Soft Tissue Calcification

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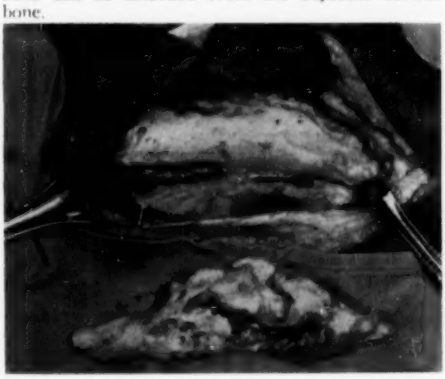
Calcification of the organic matrix of bone, enamel, dentine, and epiphyseal cartilage occurs normally in the human body. Abnormal or heterotopic sites of calcium deposition are not infrequently encountered. These deposits may be in the form of bone, or they may be a collection of calcium phosphate (apatite) crystals in an amorphous organic matrix (Robinson). Even though the exact mechanisms by which these abnormal calcific deposits are formed are not well understood, their relationship to certain disease processes has long been recognized. The obvious defects in our knowledge of the production mechanisms for heterotopic calcification and bone formation have made it impossible to rationally apply prophylactic methods in these problems and have limited the development of therapeutic measures. Included in this lack of knowledge is the mechanism by which calcium is transformed from the soluble phase in the circulating blood to the solid or crystalline phase found in calcifications in soft tissues.

Progress has been made in the knowledge of bone formation, and many investigators have made significant contributions. Robinson and Watson have pointed out the orderly relationships between the organic and inorganic components in bone matrix. They have stated that, in general, bone cells produce an extracellular organic matrix which, when once formed, sequesters crystals of calcium and phosphorus, if the blood level of these two components is within normal range, and deposits them in this matrix in a given spatial relationship to the collagen fibers and the cement substance. Bone cell

Fig. 1A.—Extensive myositis ossificans, duration one year, which interfered with normal function of knee. Since this occurs in relation to normal bone and periosteum, the possibility of new bone formation by induction must be considered.

Fig. 1B.—At operation, the heterotopic mass of bone can be detached from the adjacent normal bone.



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From the Department of Surgery, Washington University School of Medicine.

Fig. 1C.—One year after surgery, there has been a mild recurrence of the abnormal bone.

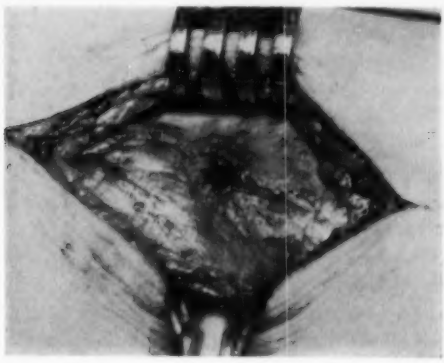
Fig. 2A.—True heterotopic bone formation far removed from normal bone structure. This was located in the sartorius muscle.

multiplication with secondary production of extra bone tissue may be stimulated by proximity to a fracture, by an osteoid osteoma, and in other ways. Such stimuli involve bone cells already present in a region where bone is normally supposed to form.

Heterotopic bone formation is, in theory, considered to be bone formation developing without association with any normal site of bone formation. This is encountered in myositis ossificans (Fig. 1) more frequently than in any other clinical problem. However, this bone formation usually occurs in conjunction with a deep-seated hematoma adjacent to bone or periosteum. This proximity of the abnormal site of bone formation to a normal site (Fig. 1) raises a question as to whether this may represent bone formation spreading out from a disrupted periosteum (a tissue rich in osteoblasts) or whether it is due to a metaplasia of connective tissue cells in the area surrounding the bone.

There are instances in which ossification occurs in a muscle (Fig. 2*A*) far removed from its bony attachment and distant from any bone. If such lesions are explored within a few months after injury, a cyst will usually be found, filled with serum and old blood (Fig. 2*B*) which resulted from the original trauma. This cyst is invariably surrounded by a thick fibrous tissue wall (Fig. 2*C*), and the bone deposition occurs in this fibrous tissue capsule (Fig. 2*D*)

Fig. 2B.—At operation, five months after the injury, a cyst filled with old blood was encountered.



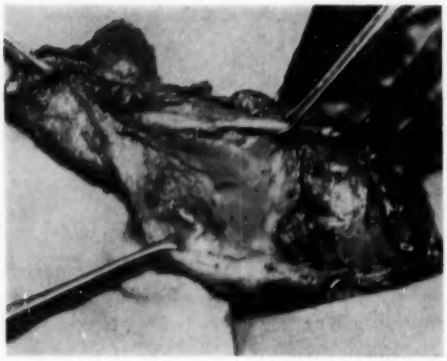


Fig. 2C.—The cyst has a distinct living membrane and is surrounded by a thick fibrous tissue wall.

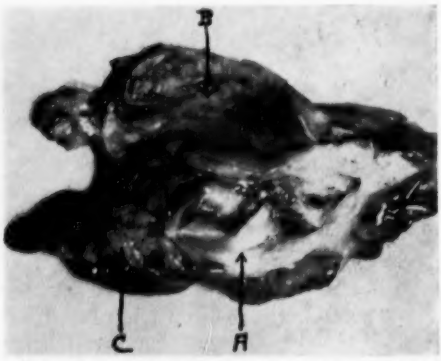


Fig. 2D.—New bone formation is found only in the surrounding fibrous tissue wall (*A*), not in the living membrane (*B*) or in adjacent muscle fibers (*C*).

rather than in the cyst's lining membrane or in the muscle fibers peripheral to the fibrous wall of the cyst. Heterotopic bone formation, distant from any normally occurring bone tissue, occasionally develops in the abdominal wall following surgery and in the extremities of patients with varying degrees of venous stasis. This has been reported by Moberg, and a series of three such cases has been accumulated by Porporis. Heterotopic bone formation has also been reported in the ovary, in uterine fibroids, and adjacent to calcified tubercles, atheromatous plaques, and renal calculi. It has been frequently found in the meninges and has been reported in carcinoma of the skin, scleroderma, periarteritis nodosum, the Fallopian tube, and teratomata.

True heterotopic bone formation, experimentally or clinically, apparently occurs only in conjunction with connective tissue structures. If heterotopic bone forms in close relationship to normal bone structures, the new bone formation by direct spread from the normal bone may be possible. In those instances, however, in which the bone formation occurs in remote portions of the body, where direct contact with bone or periosteum is lacking, one must assume that osteogenesis is dependent on some specific stimulus, either living or inert, which may be called an "inductor" (Urist and McLean). The accumulated experimental material indicates that this represents a specific cell stimulation, but the exact nature of the stimulus or "inductor" remains unknown.

Amorphous calcification in soft tissue structures is more frequently encountered in clinical experience than heterotopic bone formation. In some instances, bone formation occurs in conjunction with the calcium deposit or adjacent to it, but in many instances amorphous calcification alone is encountered. Soft tissue calcifications are frequently encountered in problems resulting from traumatic and degenerative changes. It is often difficult to differentiate between these two types of involvement, and the two may actually coexist in any patient. Those most frequently encountered involve tendons, bursae, and periarticular structures, as exemplified by calcification in the floor of the subdeltoid bursa, in the tendinous structures of the rotator cuff of the shoulder. Such calcification may actually exist in the bursal sac but probably has its origin in one of the tendinous structures, usually the supraspinatus. Codman, in his classical work on the shoulder, stated that the initial lesion in this problem consisted of degeneration of the tendon fibers of the rotator cuff. He believed the initial calcium was deposited in the degenerated portion of the tendon and gradually worked its way to the surface rupturing into the bursal sac. He felt that repeated minor trauma may be a factor in this original degenerative change.

Fig. 3A.—Acute subdeltoid bursitis of eight hours' duration in which there is no x-ray evidence of abnormal calcification.

Fig. 3B.—On aspiration of the obviously distended bursal sac, five cc. of thin, milky fluid was obtained. Two cubic centimeters of hydrocortisone (Hydrocortone) was injected, and the symptoms entirely disappeared within a few hours.

Fig. 3C.—Centrifuging the aspirated fluid produced a precipitate measuring approximately 15% by volume. Calcium content of the precipitate was found to be 6 mg. per 100 cc. and of the supernatant liquid to be 1 mg. per 100 cc., a total calcium content of 7 mg. per 100 cc., obviously too low to cast a shadow by x-ray.

Fig. 4.—Acute subdeltoid bursitis of three days' duration in which the aspirated material revealed a calcium content of 53.5 mg. per 100 cc.

It has been interesting to attempt to correlate this theory of origin with the rate or degree of calcification and with the actual percentage of calcium found in the removed material. It is a well-known fact that in acute subdeltoid bursitis it may occasionally be possible to aspirate fluid from the bursa during the first few hours or first few days of symptoms. As time progresses and organization of the inflammatory process increases, however, actual aspiration of calcific material becomes more difficult. In acute subdeltoid bursitis it has been found that the calcium content of the aspirated or excised material usually varies with the duration of symptoms in the majority of patients. For example, in one patient with symptoms of only eight hours' duration and with no x-ray evidence of soft tissue calcification (Fig. 3*A*), 5 cc. of thin, milky fluid (Fig. 3*B*) was aspirated from the subacromial area. The calcium content of this fluid was reported as 7 mg. per 100 cc. On centrifuging the fluid, a white precipitate was obtained (Fig. 3*C*), measuring approximately 15% by volume; this consisted primarily of white blood cells and cellular debris. The calcium content of the supernatant fluid was found to be 1 mg. per 100 cc. and of the precipitate to be 6 mg. per 100 cc. In another patient with symptoms of approximately three days and with x-ray evidence of calcification (Fig. 4), the fluid aspirated from the calcific deposit was considerably thicker, and the calcium content was reported as 53.5 mg. per 100 cc. In another patient in whom acute symptoms had been present for approximately one week (Fig. 5), the fluid aspirated was extremely thick and difficult to obtain. The calcium content of this material was reported as 366 mg. per 100 cc. In one patient with symptoms of two weeks' duration (Fig. 6), aspiration was successful, and the calcium content of the removed material was reported as 1800 mg. per 100 cc. In three other patients, in whom aspiration was unsuccessful and in whom acute symptoms had been present for 7 to 14 days (Fig. 7*A*), surgery was resorted to, and calcium determinations were made on the excised calcified

Fig. 6.—Heavy calcification in subacromial area, with acute symptoms of two weeks' duration, in which calcium content of aspirated material was found to be 1800 mg. per 100 cc.

Fig. 5.—Moderately heavy calcification, with acute symptoms of one week, located low over the tuberosity and perhaps in relation to the tendon of the subscapularis or teres minor muscles. The aspirated fluid revealed a calcium content of 366 mg. per 100 cc.

Fig. 7A.—Acute subdeltoid bursitis of two weeks' duration in which aspiration was unsuccessful and conservative therapy afforded no relief of symptoms.

material. This material was very thick and of the consistency of toothpaste (Fig. 7*B*). The calcium content of the material in these three patients varied between 1200 and 1800 mg. per 100 cc. In each instance the calcium content was based on the wet weight of the material removed.

It seems reasonable to conclude from these findings that, with the acute degenerative process in a tendinous structure, serum is poured out very rapidly. A secondary inflammatory change takes place, in which there is an outpouring of white blood cells and necrosis of adjacent cellular structures. These are responsible for the large amount of cellular debris found in the centrifuged aspirated material. Calcium is not poured out immediately, but its deposition begins within a few hours. From information derived in this group of patients, it would seem that this calcium deposition takes place rapidly within the first few days. As organization of this material progresses and the excess serum is absorbed, it is transformed from a true liquid to a more solid phase. In older lesions of this type in which surgery has been resorted to, it is not uncommon to find granules of sand-like material deposited in the supraspinatus tendon. Calcium determinations have not been made in these, since none has been encountered at the time of surgery since this study was begun.

Knowledge of this underlying pathologic process indicates that the commonly used methods of therapy have a rational basis, as reported by Pedersen and Key. It is well known that calcium deposits may disappear spontaneously, and this may occur as a result of diathermy or roentgen-ray therapy. This suggests an acceleration of the healing process by increased vascularity and secondary inflammatory changes. Since the underlying pathology consists of primary fibrous tissue degeneration, the injection of hydrocortisone (Hydrocortone) has a rational basis and frequently relieves the symptoms. This may succeed with or without the aspiration of collected fluid. Roentgen-ray therapy has been used much longer than hydrocortisone and, in a group of approximately 50 acute cases so treated, has

Fig. 7B.—At operation, thick tooth-paste-like material was obtained on opening the bursal sac. Some calcification was also found in the supraspinatus tendon; calcium content of this material was found to be 1800 mg. per 100 cc.

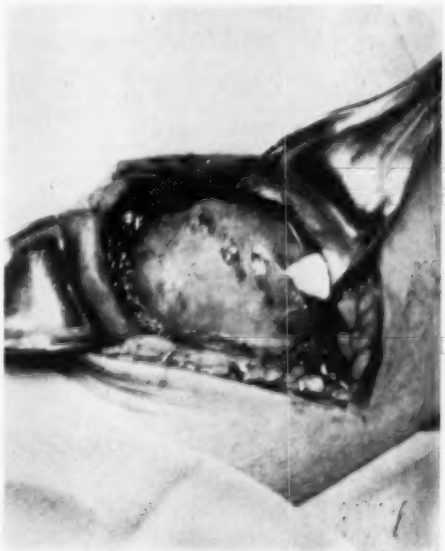


Fig. 8A.—Calcinosis universalis in a 15-year-old boy in whom the initial symptoms appeared at 3 years of age, with acute joint disease followed by progressive thickening and hardening of soft tissue.

Fig. 8B.—The calcification is limited to the hamstring muscles on the posterior surface of each thigh.

succeeded in relieving the acute symptoms in approximately 40%. Hydrocortisone has been used for too short a time to permit a definite statement with reference to its efficacy, but it is probably successful in approximately the same percentage of cases. Both of these conservative types of treatment should be used before surgery is resorted to. If, however, in spite of these measures the acute symptoms persist or the symptoms are severe enough to warrant further therapy, surgical intervention and surgical excision of the bursa and of the area of calification should then be considered. It should be remembered that, when the area of calcification in the supraspinatus tendon is quite large, total excision of the area of involvement may impair the function of the supraspinatus muscle. Calcium deposits may occur in any of the tendinous structures constituting the rotator cuff of the shoulder, although they are less frequent in the tendons of the teres minor and the subscapularis than they are in the superior tendinous structures.

Fig. 8C.—The hamstring tendons of the right thigh were explored in an attempt to correct a flexion deformity of the knee; here we see extensive calcium deposit in the sheath about the semitendinosus tendon with some secondary scarring of the tendon.

Fig. 8D.—In the sheath of the biceps femoris tendon, there is heavy rock-like calcium deposition with secondary scarring of the tendon.

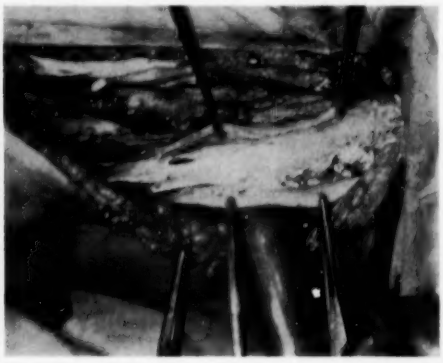


Fig. 8E.—On dissecting proximally into muscle, amorphous calcification (*A*) was found in the surrounding fibrous tissue sheath, and the muscle belly itself showed no involvement; there was no evidence of ossification.

Amorphous soft tissue calcification has occasionally been mistakenly classified as progressive myositis ossificans. A classical case of this type has been seen and studied. The initial onset of symptoms apparently occurred at approximately 3 years of age, at which time there was evidence of acute joint disease followed by limitation of joint motion and increasing thickening and hardening of the soft tissue structures of the extremities. At the time of my initial examination at the age of 15 years, the patient showed evidence of massive calcification in both thighs, but the involvement was limited to the region of the hamstring muscles on each side (Figs. 8*A* and 8*B*). There was also involvement about the pelvis, the back, the triceps muscle in each upper extremity, and about one shoulder girdle. There was some involvement of the muscles below the knee, but this was extremely mild in degree. At the age of 18 years, the hamstring tendons on the right were explored and sectioned in an attempt to correct a fixed flexion deformity of the knee. The calcium deposits were found to be within the tendon sheaths and with some involvement of the tendinous structures (Figs. 8*C* and 8*D*). Following the tendons proximally into the muscle, it was found that the muscle structure remained perfectly normal. The calcium deposition at this level had taken place entirely in relation to the fibrous tissue sheath surrounding this muscle belly (Fig. 8*E*). Some of this material was removed for study. No paste-like calcium material was encountered, and in this late stage the calcium deposition existed in the form of gravel and sand. Biopsy of the muscle bellies showed no evidence of involvement of muscle structure. It would seem, therefore, that the term myositis ossificans in such problems is not accurate or descriptive. This was not ossification but rather amorphous calcification which occurred in adjacent or surrounding fibrous tissue structures and not within the muscle itself (Fig. 8*F*).

Striking examples of soft tissue calcification are often classified as calcinosis localisata or calcinosis universalis, sometimes accompanying dermatomyositis. A patient of this type was admitted to the St. Louis Childrens Hospital in 1948 at the age of 3 years. She was admitted on the service of Dr. A. F. Hartmann who has since directed her studies and treatment. Shortly prior to admission, the child had an acute onset of symptoms with fever, swelling, pain, and redness of multiple joints. Her family physician made a diagnosis of acute rheumatic fever. At the time she was admitted to the hospital the acute process had subsided somewhat, but the child still had a low-grade fever and slight swelling of multiple joints. It was then felt that this represented a relatively acute type of diffuse rheumatoid arthritis (Figs. 9*A*, 9*B*, and 9*C*). This child was treated symptomat-

Fig. 8F.—Photomicrograph showing amorphous surface calcification with no involvement of muscle substance.

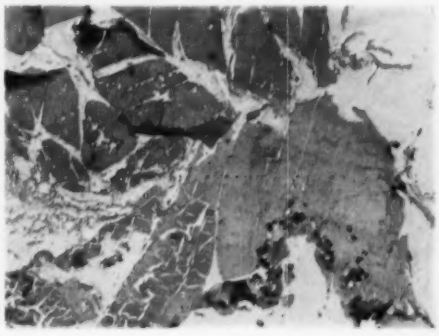
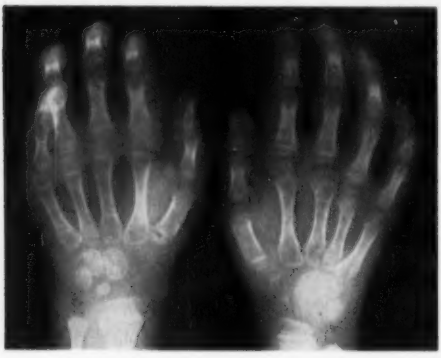


Fig. 9A.—Three-year-old girl with acute joint symptoms suggestive of rheumatic fever or acute rheumatoid arthritis; except for demineralization there is no evidence of abnormality.

ically over a period of approximately two years, during which she showed progressive soft tissue changes which suggested the possibility of lupus erythematosus and, still later on, a diffuse type of dermatomyositis (Fig. 9*D*). Calcification appeared in the soft tissues approximately two years after the onset of symptoms. At this time the diagnosis was changed to diffuse dermatomyositis with calcification or calcinosis universalis, as preferred. Since it was felt that this represented a primary connective tissue degenerative process associated with one of the collagen diseases, corticotropin therapy was instituted in this child on June 14, 1950.

Fig. 9C.—After two years, there was extreme demineralization in the bones of the hands and diffuse soft tissue thickening but no evidence of abnormal soft tissue calcification.



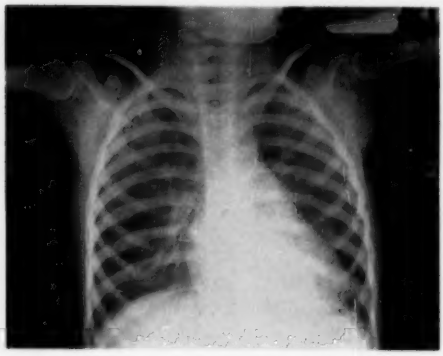


Fig. 9B.—The chest film showed no evidence of adjacent soft tissue calcification.

Fig. 9D.—During the first two years, there was progressive soft tissue thickening and scarring and the diagnosis was changed to dermatomyositis. Shortly after this, calcium deposits appeared in the soft tissue, and the diagnosis was changed to calcinosis universalis or dermatomyositis with calcification. At this time corticotropin therapy was begun with administration of 10 mg. every 6 hours for 35 days, then once daily for 3½ years.

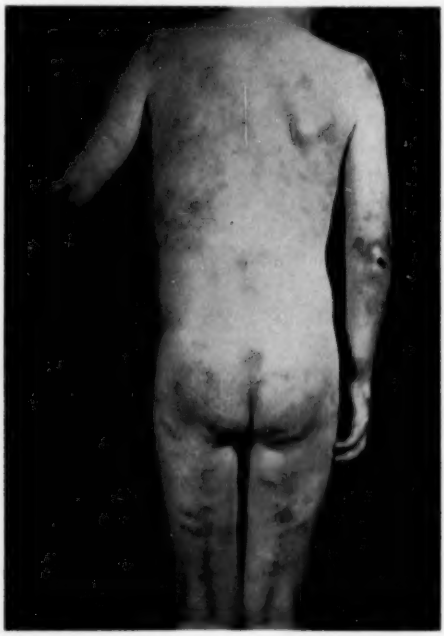


Fig. 9E.—In spite of definite clinical improvement, the soft tissue calcification progressed; this shows A. P. view of knees 5 years after corticotropin therapy was begun (compare with Fig. 9A).

Fig. 9F.—Extensive calcification about the thorax five years later (compare with Fig. 9B).

Fig. 9G.—Five years later, there is massive soft tissue calcification in the hands (compare with Fig. 9C); this could represent progressive tissue degeneration and calcification in spite of hormone therapy or a healing phase of the process in tissues damaged prior to the institution of therapy.

Fig. 9H.—Photograph five years after the institution of hormone therapy and five years after Fig. 9D; note the large subcutaneous masses of amorphous calcification; tooth-paste-like material obtained from two of these revealed calcium content of 1500 mg. per 100 cc. and 1600 mg. per 100 cc.

Ten milligrams was given every six hours for two weeks during her hospital stay. After returning to her home, the drug was continued at this level for approximately 23 days. During this time there was marked clinical improvement. A maintenance daily dose of 10 mg. of corticotropin was then continued for three and one-half years. During the early part of this period the child continued to improve clinically, but during the last year of corticotropin therapy a base line was apparently established. After the corticotropin therapy was discontinued, she was given cortisone for a time without any additional alteration in her findings, and therapy was gradually discontinued. She now has had no drug therapy for four months, and during this time there has been no further increase in symptoms. In addition to the areas of calcium deposition in the deeper tissues, these patients exhibit soft tissue calcification in subcutaneous tissues. Two such areas in this child opened and drained spontaneously, and the soft paste-like calcium material was studied for calcium content. One of these was reported as 1500 mg. per 100 cc. and the other as 1600 mg. per 100 cc. These calcium deposits had been present for a long period of time, and this undoubtedly explains the high calcium content. In spite of the fact that corticotropin therapy resulted in clinical improvement in this patient, progressive soft tissue calcification continued over a period of at least two years after the institution of specific therapy (Figs. 9*E*, 9*F*, 9*G*, and 9*H*). It is possible that this could represent further progressive tissue degeneration and calcification in spite of hormone therapy, but it is also possible that, since the child showed evidence of clinical improvement, this could represent a healing phase of the process in tissues damaged prior to the institution of therapy.

Comment

It seems obvious in the light of our present knowledge that problems of abnormal soft tissue calcification may, in many instances, be related to the over-all problem of collagen diseases and result from primary degenerative changes in connective tissues. Calcinosis universalis represents widespread calcium deposition in fibrous or connective tissue structures in which degenerative changes have resulted from a systemic disease process. In other more localized types of soft tissue calcification, primary degenerative changes may serve as the etiological factor, but many of these may result from trauma to tendinous or fibrous tissue structures.

Permission to include his case of calcinosis universalis was granted by Dr. A. F. Hartmann. Dr. Robert A. Robinson offered many helpful suggestions in the preparation of the paper, and Mr. Cramer Lewis supplied the illustrations.

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Traumatic Rupture of the Thoracic Aorta

Report of a Case

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The literature is replete with articles and case reports concerning all types of injury to the aorta. Open trauma, by its very nature, is readily recognized and is often approached positively. The lack of aggressive attack in cases of closed injury to the aorta is probably due to several factors. First, one must be familiar with how the injury occurs,[1,5,12] where it occurs,[5,12,10] and how it is manifested.[2,14,16] Knowing these basic things, one can make the diagnosis. Secondly, one must comprehend the variety of injuries[1,3,5,11,12] possible and the principles of vascular surgery[2] which may be brought to bear in the individual case. When one has these facts at hand, a rational plan of therapy may be evolved.

Closed injury to the aorta usually results from a combination of forces acting on the dynamic blood column within the thorax. The forces are (1) inertia, or "drag," in sudden deceleration[3,12] and (2) compression with momentary disruption of open circulation. The force of inertia is exerted directly or in a torsional plane (rotary contrecoup) on the blood column, the frictional forces of which produce wrinkles, tears, or "cracks" in the intima. Should the simple direct weight be exerted strongly enough against "fixed points," a shearing effect may be produced, and complete transection of the aorta may occur.

Compression, by its momentary stoppage of cardiac outflow, may produce an effect on the aortic wall similar to that produced by squeezing a "full-blown" balloon. Again, the graduation of injury is from an intimal tear to complete disruption.

Where does one find the above combination of forces? Practically, in the so-called "steering-wheel" injury.

Recalling simple anatomic facts about the aorta in the light of the foregoing facts, one can readily see why most of the injuries are located (initially) just distal to the aortic valve or, even more frequently, just distal to the ductus Botalli.[2,5,10,11] A few occur in the descending aorta.[10] The points of "fixation"—heart, ligamentum arteriosum, intercostal vessels, etc.—permit the forces acting to concentrate in the very areas where injury is usually found. In addition, in the valve area the timing of the forces in relation to the opening and closing of the valves is thought to be important. Also, there is believed to be a "rocking" force in the most proximal aorta, exerted by this same valve action,[7] which further reduces structural stability. Abbott, as cited by Kastl,[5] points out the probability of a congenital weakness of the aorta just distal to the ligamentum arteriosum.

The injury usually has its inception in the posterior intima.[9] No ready explanation of this is at hand, unless one calls on the forces of friction and inertia. As the column of blood is thrown forward, so to speak, the greatest force is borne by the dorsal arc of the aortic semicircle, and the tissue gives way.

How does the injury manifest itself clinically? Should the injury be near the aortic valve, various aortic valvular murmurs may be heard.[7] Pain will be that of coronary occlusion and/or dissecting aneurysm.[6,14]

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At the time this case was treated, Lieutenant (MC), U. S. Army; now Resident in General Surgery at the University of Arkansas Medical Center, a trainee of the National Cancer Institute.

There may be aberrations, nonspecific, or peripheral pulses. The ECG may show varied evidence of heart strain but nothing more.[18] The plain radiogram may show widening of the mediastinum and/or "layering" and lamination or simple widening of the aortic shadow in the lateral projection.[16] Unexplained anemia may suggest undetected bleeding and, in conjunction with other findings, is significant.[2,5] Instability of vital signs is extremely variable; shock may be but a terminal event. Occasionally, associated injuries will be suggestive. For example, fracture of the sternum, particularly the manubrium, is often associated.[6] On the other hand, associated injuries, multiple, extreme, are common, and all too frequently take the case out of the physician's hands.

At postmortem examination the injured aorta may be entirely healthy in all respects, or it may present the lesions of atherosclerosis, the medial necrosis of Erdheim, or the "hyaline fibroid" lesion of Adami.[9] Apparently prior disease is not a significant factor in injury, though it may be in prognosis.

The injury most frequently is primarily an intimal and partial medial tear with the subsequent development of a true dissecting aneurysm. Less commonly, the tear extends nearly to adventitia, and a saccular aneurysm results. Rarely (in survivors) a complete tear or even a transection may form a pseudoaneurysm with temporary survival[5,8]; this "false" aneurysm may be saccular or fusiform, depending on whether the vessel is partially or wholly transected. Secondary rupture with exsanguination is the common cause of death. A very frequent fate of the more proximal dissecting aneurysm is cardiac tamponade following rupture into the pericardial sac. Survival periods in these injuries are extremely variable,[2,5,8,10,13] depending on the patient's tissues, site of injury, and extent of injury. Suffice it to say that enough patients survive long enough to make this an urgent surgical problem.

The various surgical approaches to the above lesions are described in many excellent articles and case reports.[2]

Report of Case

A 23-year-old white man was admitted to the U. S. Army Hospital, Fort Leonard Wood, Mo., at 8:30 a. m., March 15, 1955, approximately two hours after injury in an auto accident. It was ascertained that the accident was a head-on collision of two automobiles and that the patient, a driver, was pinned by the steering wheel of his car. The patient complained bitterly of substernal compression and dyspnea and severe pain in the left hip. Very little detail of history could be given, as the patient suffered moderate cerebral concussion at the time of impact.

Examination.—The patient was obviously in acute respiratory distress, cyanotic, extremely anxious, and restless. B. P., 80/60; P., 150. The positive physical findings were limited to the thorax and the left hip. There was diminished respiratory excursion on the right, and the breath sounds were diminished over the right apex; rales were detected in both lung bases. No cardiac or mediastinal abnormality was detected. The left hip was tender and presented moderate limitation of motion. Inasmuch as the patient had sustained thoracic crush and complained so extensively of substernal compression, an ECG and a medical consultation were requested, along with chest films, etc. The ECG revealed elevation of the R-ST segment in Leads I, II, VV, and VVI, the significance of which was not readily recognized. The medical consultant detected no unusual heart tones, murmurs, etc. The initial chest film revealed a 20% pneumothorax on the right with a widened superior mediastinal shadow (interpreted as due to hemorrhage) and interstitial pulmonary hemorrhage in the right lung base. No rib fractures were noted. Pelvic films revealed a linear fracture of the left inferior pubic ramus, in good position. Concomitant shock therapy had elicited little response to 1000 cc. of dextran and 500 cc. of whole blood. A repeat chest film (one hour after admission) revealed 40% pneumothorax on the right, perhaps a slight increase in the mediastinal widening, and interstitial hemorrhage in the left lung base. Right anterior thoracostomy with water seal drainage was immediately instituted. After this and injection of 500 cc. more of whole blood, the blood pressure was 120/80; the pulse, 100. Some two hours after admission the patient was stable, of good color, and complaining constantly of substernal compression. Again, the cardiovascular status was checked. Pulses were good and equal throughout; cardiac tones, good; no murmurs were heard.

Laboratory findings on admission: RBC, 3.18; Hgb., 10 gm.; Hmt., 28%, and WBC, 26,000. N. P. N. was reported 33 mg. per 100 cc. and the CO_2 combining power, 51%.

The evident anemia was not adequately explained. However, in the absence of a positive diagnosis a conservative program was embarked upon.

March 16, 1955: A chest film revealed a fluid level in the right chest. Hgb. was 8 gm. Thoracentesis produced 230 cc. of blood.

March 16-19, 1955: Condition was stable except for intractable anemia, for which blood was given p. r. n.

March 19, 1955: A chest film showed bilateral pleural effusions. Thoracentesis yielded 850 cc. of blood from the right chest and 675 cc. of blood from the left chest. Again, transfusion was resorted to. It was evident at this point that a major vascular injury had occurred. The widened mediastinum and bilateral hemothorax pointed out that this was in the mediastinum. Physical examination was not revealing. Inasmuch as the patient was adequately maintained conservatively, it was believed that the vascular damage must perforce have been venous and probably would ultimately cease spontaneously. But on March 20, 1955, 475 cc. of blood was removed from the right chest and 1000 cc. from the left chest. Thoracotomy was considered, and the decision made to wait another 24 hours; 4000 cc. of blood had been given to combat anemia.

March 20-24, 1955: The chest film remained clear and evidenced improvement in the mediastinal shadow. The hemogram remained constant.

March 24, 1955: The patient complained of soreness through the chest, perhaps a little severer than usual. Aside from a low-grade fever, the patient was apparently in satisfactory condition.

March 25, 1955: Condition was stable. The patient was ambulated. The prominent complaint at this time was pain throughout the thorax. About 3 p. m. the patient complained of substernal compression and epigastric cramps. The patient was returned to bed, and vital signs checked; a barium swallow was scheduled, as dysphagia was noted. At 5 p. m. there was an abrupt crescendo of substernal compression with extreme dyspnea, followed momentarily by a massive diffuse enlargement of the anterior neck. The precordium developed a paradoxical movement; the mediastinum was percussably widened, but no other changes were noted. A tracheotomy was performed, and a chest film obtained. The chest film revealed a marked widening of the superior mediastinum and a "knob-like" shadow in the region of the left pulmonary hilum. The situation could only be assessed as desperate, and immediate thoracotomy was planned. The preoperative diagnosis was rupture of a great vessel at or just distal to the base of the heart.

Operative Note.—A thoracotomy through the left fourth intercostal space was carried out. The pericardium was examined, as was the anterior mediastinal pleura. The former was incised, and exploration carried out. Nothing was found. The left lung was then drawn anteriorly, exposing at the pulmonary hilum a 4-6 cm. hemispherical mass, deep blue in color, pulsating, with a palpable thrill. In short, this was obviously blood under high pressure and great tension. The exact nature of the lesion was undetermined; however, time being a factor, it was immediately decided to place occlusive tapes well above and below the evident pathology. The pleura posterior to the aorta, and away from the mass, was incised and reflected anteriorly. It was at once apparent that a similar incision would be required anteriorly. This was carried out. In attempting to further mobilize above and below the lesion, a sudden gush of blood initiated a massive uncontrolled hemorrhage, which exsanguinated the patient. A left pneumonectomy was done as a desperation measure in hopes that this would expose the origin of the hemorrhage; it did not.

A brief postmorten dissection revealed a complete transection of the aorta, just distal to the ligamentum arteriosum, with a large pseudoaneurysm of the mediastinum. A cuff of partially organized blood clot embraced the severed ends of the aorta.

A gross autopsy added the following: fracture of the sternum; extensive mediastinal hemorrhage, old and recent; massive retroperitoneal hemorrhage; lacerations (multiple) liver and spleen (not actively hemorrhaging), and renal contusion. Also, a small (7 mm.) posterior through-and-through laceration of the aorta at T-8 was encountered. This lay against the vertebral body and was not considered a prime source of hemorrhage by me. Microscopic studies are not available.

In summary, the case was interpreted as complete transection of the aorta with extensive mediastinal hemorrhage, followed by partial organization of clot immediately about the site of separation (forming a false aneurysm), which was partially effective in correcting the injury. A secondary rupture of this pseudoaneurysm initiated the final progression of events.

Comment

This case is remarkably reminiscent of the one reported by Kastl.[5]

A false aneurysm in this location presents formidable problems in accurate localization and surgical attack.

Aortography, angiography, etc., do not offer safe accurate techniques for this type of patient at this time.

Several factors led to error in the management of this case. Primarily these were prolonged survival, normal femoral pulses, and bleeding which was believed gradual and hence most likely venous. Here, again, are factors which were confusing in Kastl's case.[5]

Emphasis must be placed on these points: steering-wheel injury; pain simulating coronary occlusion; hemothorax (especially without rib fractures); radiographic widening of the mediastinum, and disparity in known blood loss and degree of anemia.

It is suggested that this type of lesion be urgently sought for, no matter how improbable it may seem, in all cases of deceleration injury, most especially if associated with thoracic compression.

Summary and Conclusions

A case of traumatic rupture of the aorta is reported. The clinical picture evolved is typical of this lesion.

Causes of diagnostic error are noted, and significant points in correct interpretation of clinical findings are emphasized.

Severe closed injury to the thoracic aorta can and should be diagnosed in a good percentage of cases when it has occurred.

Survival periods in these patients, often surprisingly prolonged, create a pressing problem for the surgeon.

Safe, accurate means of positively identifying and localizing these injuries are needed.

R. W. Buchanan, M.D., of Summit, N. J., and George E. Block, M.D., of Chicago Clinics, assisted in the management of this case.

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Postgastrectomy Retention

Treatment by Second Gastroenterostomy

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In view of the fact that the logical treatment of stomach obstruction after gastrectomy is based on its pathogenesis, a brief review of the causative factors of this not infrequent complication seems justified.

Malfunction of the stoma may be of functional or organic origin.

There is a lack of agreement about the character of functional disturbances. One school of thought [1,2] voices the belief that a spastic contraction of the efferent loop may be due to "pseudovagotomy," created by cessation of the sympathetic function. Conversely, another group [3] holds the view that postoperative gastric atony may play a considerable part in retarded emptying of the stomach. Ravdin [4] pointed out that a low colloid osmotic pressure, due to hypoproteinemia, may give rise to edema of the suture line and that the coincidental dehydration may mask the serum protein deficiency.

An organic obstruction may be created by one of the numerous factors: (1) localized peritonitis with abscess formation or a hematoma in the lesser peritoneal sac; (2) a constricting ring produced by inverting excessive amounts of tissue in performing the anastomosis; (3) a spur at the anastomotic site, formed by the festooning descent of the afferent and efferent jejunal limbs; (4) angulation or torsion of the efferent loop, attributable to adhesions between the efferent loop and the denuded pancreas; (5) intussusception of the efferent loop [5] brought about by an increase of the abdominal pressure in course of vomiting; (6) herniation of the anastomosis upward through the transverse mesocolon, and (7) compression of the efferent loop by an abnormally short mesocolon, especially if the stoma lies to the right of the middle colic artery.

The differential diagnosis of both groups of stomal obstruction is based chiefly on the observation that the functional type makes its appearance during the very early stages of the postoperative period, whereas organic disturbances first become noticeable a few days after the operation. As a rule, the character of an organic obstruction can be determined only at the second exploration.

Malfunction of the stoma developing in course of the first few postoperative days should be treated conservatively, with special attention to gastric decompression, intravenous alimentation, and electrolyte balance.

If the symptoms do not subside within reasonable time and the clinical suspicion of an organic obstruction is supported by roentgenologic findings, palliative treatment should not be continued indefinitely, because procrastination may lead to a rapid deterioration of the patient's condition.[6]

A logical approach to the relief of an organic obstruction would consist of an attempt to eliminate the responsible factor. For instance, a hematoma or an abscess could be evacuated and drained. If a stomal spur is found, the sharp angulation of the two limbs of the jejunal loop can be corrected by suturing the bowel to the stomach for some distance on either side of the stoma or by performing jejunoplasty.[7] Three methods are at our disposal in the

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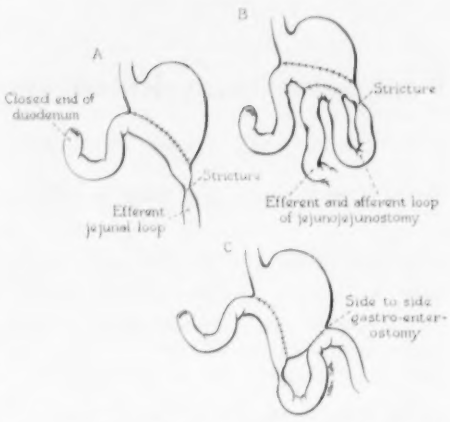
treatment of a kink or volvulus of the efferent loop: (1) direct attack on the obstruction, namely, severing adhesions responsible for the condition; (2) sidetracking enteroanastomosis between the afferent and efferent loop and the segment of the efferent loop just below the stricture, and (3) duodenojejunostomy performed in the same manner. If an intraluminal ridge produces obstruction, the anastomosis can be taken down and reconstructed after excision of the constricting ring. A hernia of the stoma can be corrected by pulling it down and attaching the mesocolon to the stump of the stomach above the anastomosis. Jejunostomy for feeding purposes is rarely indicated, because its usefulness is based on the assumption that the obstruction is of a transient character and will subside in course of time.

Great technical obstacles may render such procedures extremely difficult. Not only can the orientation be impaired by numerous adhesions, but the danger of traumatizing the pancreas should be kept in mind. Warren,[8] Lahey,[9] and others have warned of the hazards of pancreatitis following the damage of the organ. Furthermore, a careful peritonealization of raw surfaces does not always prevent formation of new adhesions. An enteroenterostomy between the afferent and efferent jejunal loop just below the constriction deprives the stomach of the neutralizing effect of the alkaline bile and the duodenal and pancreatic secretion and is conducive to the development of a marginal ulcer.

To obviate the aforementioned shortcomings of the customary methods of treating gastric retention, especially the one due to a stricture of the efferent loop, one of us (J. K. N.)[10] suggested the use of the stomal portion of the jejunum (Fig. *B*) for a new jejunojejunostomy instead of the afferent loop. This method is particularly valuable if the proximal loop is very short or is adherent to the adjoining tissues.

Should the stomal region be enveloped by numerous adhesions, it may be preferable to abstain from an attempt to liberate the anastomotic region and to perform a second gastroenterostomy proximal to the first (Fig. *C*). This procedure, combined with Braun's enteroanastomosis between the new afferent and efferent loop, has been advocated by Vullief, Hansen, Neugebaur, Finsterer, and others.[11] We found that in such cases enteroanastomosis is superfluous and that a second gastroenterostomy alone may relieve the obstructive symptoms.



A, stricture of the efferent loop. *B*, bypassing the stricture by establishment of a new communication between the stomal portion of the jejunum and jejunal segment distal to the stenosis. *C*, a sidetracking second gastroenterostomy.

The following case illustrates the employment of this method and substantiates its usefulness.

A Polya type of subtotal gastric resection with retrocolic gastrojejunostomy was performed in St. Elizabeth Hospital on a 66-year-old man with pyloric obstruction due to an ulcer. According to the attending surgeon's statement, the first three days after the operation the patient was responding well to the routine treatment. When the decompression was discontinued on the fourth postoperative day, he began vomiting. The Levin tube was reinserted, but clamping it off continued to cause nausea. X-ray studies on the sixth postoperative day revealed an obstruction of the efferent loop, with the stomach pouch greatly distended.

An exploratory celiotomy was performed on the 12th postoperative day. A constriction of the efferent loop, approximately 2.5 cm. below the stoma, was found. Dense adhesions were present in the entire area, making the stomal region inaccessible. To avoid further trauma, unavoidable

in the exposure and liberation of the afferent and efferent loops, a second antecolic gastroenterostomy proximal to the first was performed, leaving the involved area intact. An Abbott-Rawson tube was inserted into the remaining portion of the stomach and the efferent loop before placing the anterior row of sutures. Gavage was done for seven days, and the decompression was discontinued on the fifth day.

X-ray studies on the 15th postoperative day showed the remaining gastric pouch of normal size, a nonfunctioning first gastorenterostomy and a patent second stoma. The postoperative course was smooth. A follow-up study six months after the second operation showed the patient in good health, without any digestive disturbances.

Summary

Second gastroenterostomy for the treatment of postgastrectomy retention appears to have sufficient merit to warrant further consideration in selected cases in which other customary methods are contraindicated on technical grounds.

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Lumbar Sympathectomy in the Treatment of Peripheral Vascular Diseases

Comparison of Results of Two Series

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A reevaluation of our results of lumbar sympathectomy in the management of a variety of peripheral vascular diseases appears warranted at this time. Since our last survey and report on this subject in February, 1953, many other reports have appeared in the literature. Some of these have not been as favorable as those reports which had been published from 1946 to 1953.

The purpose of this report is to make a comparison of the two groups of patients with a variety of peripheral vascular diseases treated; the first group was treated during the period from October, 1946, to December, 1951 (Group A), and the second group, from January, 1952, to December, 1955 (Group B).

The primary purpose of a lumbar sympathectomy in patients with the diseases of the peripheral vascular system, included in this study, is to release vasospasm and permit a more adequate development of small, unaffected collateral channels in the involved extremities. As a result of this, the extremity is provided with some increase in circulation, which increases both the oxygen and the nutriments to the tissues and aids in the removal of tissue by-products.

The sympathectomy per se will not modify or reverse the existing pathology in the diseased vascular channels. However, the additional increase in blood supply to the distal strictures and tissues in many instances is adequate enough to maintain the integrity of the extremity and in some cases avoid the need of a major amputation, or, if the latter is necessary, frequently it will permit its accomplishment at a lower level.

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From the Department of Surgery, Veterans' Administration Hospital.

General Comparison of Two Groups

This survey involves Group A, 1946-1951, of 159 male patients upon whom 221 lumbar sympathectomies were performed and Group B, 1952-1955, of 116 male patients upon whom 170 lumbar sympathectomies were performed. Follow-up studies were obtained in the two groups at about the same intervals, as well as the over-all follow-up period. In Group A 26% of the operations were on the right side and 39% were performed bilaterally, as compared with 30% on the right side and 47% performed bilaterally in Group B. In the majority of cases when a bilateral procedure was necessary, the second or opposite side was operated on 7 to 14 days later. Bilateral procedures on the same day were accomplished more frequently in Group B.

The patients were distributed throughout the various age groups; the youngest were 20 to 21 and the oldest were 84 to 85 years of age in both groups. The greatest number were in the 51-70- and the 31-40-year age groups in both series. However, a significant increase in the older age groups was noted in Group B, being 76% as compared with 48% in Group A, whereas there was a reduction in the younger age groups, as noted in Group B, of only 10% against 23% in Group A (Table 1).

The patients were classified into the following categories: arteriosclerosis (including diabetics); arterial embolism, aneurysm,

TABLE 1.—*Classification of Diseases Treated and Age Groups*

Clinical Diagnosis	No. of Cases	Incidence by Decades							Per Cent of Total
		20–30	31–40	41–50	51–60	61–70	71–80	Over 81	
Arteriosclerosis (including diabetics)	A—49			1	26	18	3	1	30.7
	B—66			1	29	32	3	1	56.9
Arterial embolism, aneurysm, or thrombosis.	A—10	2	2	1	4	1			6.2
	B— 5	1			2	2			4.3
Buerger's disease (thromboangiitis obliterans)	A—31	5	11	5	10				19.4
	B—10	2	3	2	3				8.6
Frostbite, causalgia	A—21	11	7	1	2				13.2
	B— 8	1	5	1		1			6.9
Thrombophlebitis, chronic	A—23	4	7	4	6	1	1		14.4
	B—23	1	4	3	8	7			19.8
Varicose or chronic leg ulcer	A—11	3	4	1	3				6.9
	B— 2				1	1			1.7
Unclassified	A—14	3	5	1	5				8.1
	B— 2				1	1			1.7
Totals *	A—159	28(17.6)	36(22.6)	14(9.5)	59(35.2)	20(12.5)	4(2.5)	1(0.06)	
	B—116	5(4.3)	12(10.3)	7(6.1)	44(37.9)	44(37.9)	3(2.6)	1(0.08)	

* Percentage figures in parentheses.

or thrombosis; thromboangiitis obliterans (Buerger's disease); frostbite and causalgia; chronic thrombophlebitis; varicose or chronic leg ulcer, and unclassified (Table 1).

Patients with arteriosclerosis (diabetics included) represented the largest number in both series, with a remarkable increase in the latest series, Group B, 56.9%, as compared with 30.7% in Group A. Buerger's disease was second in frequency in Group A, whereas in Group B chronic thrombophlebitis occupied this position.

Surgical Procedure

The surgical technique employed was identical in the two groups. Lumbar sympathectomies, either single or bilateral (at the same time), were usually performed under spinal anesthesia through a transverse midabdominal incision, on either or both sides, placed at the level of the umbilicus. The approach was extraperitoneal through a muscle-splitting incision. The sympathetic ganglionated chain was removed from below the first lumbar ganglion to below the fourth. There are a variety of patterns in the formation of the chain and also a variation in the number of ganglia. The wound was closed in layers, nonabsorbable surgical sutures being used throughout. The patients were ambulatory on the first postoperative day. There were no postoperative hernias following this type of incision and wound closure. A postoperative sweating test was obtained in the majority of cases. Typical sympathetic denervation was present in the vast majority of patients, with loss of sweating below the knees anteriorly and from the sacrum posteriorly to the tips of the toes.

Results

Arteriosclerosis (Including Diabetics).—In this category there were 49 male patients in Group A (20 diabetics), ranging in age from 44 to 84 years of age. The average age was 59.2 years; the greatest number were in the 51- to 60-year age group (Table 1). Seventy-two sympathectomies were performed: thirteen, on the right; the same number, on the left, and twenty-three were bilateral.

In Group B there were 66 (19 diabetics) male patients, ranging in age from 49 to 85 years of age. The average age was 61.1 years; the greatest number were in the 61- to 70-year age group (Table 1). One hundred five sympathectomies were performed: fourteen on the right; thirteen on the left, and thirty-nine were bilateral.

The average duration of symptoms in Group A was 18 months; the shortest was one week, and the longest, 20 years. In 45 (90%) patients the major and chief complaint was pain. In association with this, 21 patients also had cellulitis, and 23 had chronic leg or foot ulcers. In seven there was edema of the extremities. In 17 patients there was gangrene of the toes, and in 1

TABLE 2.—*Symptoms and Physical Findings*

Clinical Diagnosis	No. of Cases	Pain	Ulceration	Gangrene	Cellulitis	Edema	Peripheral Pulse, Absent or Diminished
Arteriosclerosis (including diabetics)	A—49 B—66	45 46	23 19	18 16	21 19	7 7	47 46
Arterial embolism, aneurysm, or thrombosis	A—10 B— 5	10 5		2 4		2 0	9 5
Buerger's disease	A—31 B—10	29 9	5 1	5 2	1 3	5 2	28 10
Frostbite and causalgia	A—21 B— 8	18 6	6 3	4 3	3 2	2 4	14 3
Thrombophlebitis, chronic	A—23 B—23	18 16	3 12	2 1	0 11	17 22	15 7
Varicose or chronic leg ulcer	A—11 B— 2	7 0	9 2		0 1	6 1	5 1
Unclassified	A—14 B— 2	11 1	2 0		2 0	4 1	9 1

patient gangrene involved the foot also. In 47 patients there was a diminished or absent peripheral arterial pulse (Table 2).

The average duration of symptoms in Group B was 26.2 months; the shortest was one week, and the longest, 15 years. In 46 (70%) patients the major and chief complaint was pain. In association with this, 19 patients also had cellulitis, and 19 had chronic leg or foot ulcers. In seven cases there was edema of the extremities. In 16 patients gangrene of the toes or foot existed. In 63 patients a diminished or absent peripheral arterial pulse was noted (Table 2).

Amputations were performed following sympathectomy in 14 (29%) of the patients in Group A with gangrene of the toes or foot. In six the amputations were performed above the knee (one bilateral), and in five patients (two bilateral) amputations were performed below the knee. In two patients transmetatarsal amputations were performed. In two patients amputations of gangrenous toes were all that was required.

Amputations were performed in 17 (25%) of the patients in Group B with gangrene of the toes or foot. In seven the amputations were performed above the knee (two bilateral), and in six patients (two bilateral) amputations were performed below the knee. In two patients transmetatarsal amputations were performed, and in two others only the involved toes were amputated.

The postoperative follow-up evaluation indicated that results were considered good in 30 (61%), fair in 13 (26%), and poor in 6 (13%) patients in Group A and good in 41 (62%), fair in 13 (19%), and poor in 12 (18%) in Group B (Table 3).

Buerger's Disease (Thromboangiitis Obliterans).—In Group A there were 31 patients upon whom 51 lumbar sympathectomies were performed. Six were performed on the right; five, on the left; and the remaining twenty were bilateral. The youngest patient was 25, and the oldest, 59 years of age; the average age for this group was 40.7 years. The greatest number were in the 31- to 40-year age group (Table 1).

In Group B there were only 10 patients upon whom 17 lumbar sympathectomies were performed. Three were performed on the right, and seven were bilateral. The youngest patient was 23, and the oldest, 56 years of age; the average age was 40.6 years. The greatest number were in the 31-40- and the 51-60-year age groups (Table 1.)

The average duration of symptoms in Group A was 44 months; the shortest was 5 weeks, and the longest was 12.5 years. In 94% of the patients the major and chief complaint was pain. In association with this, five patients had edema or an ulcer or both; one had cellulitis, and five had gangrene of one or more toes. In 28 of the 30 patients a diminished or absent peripheral pulse was noted (Table 2).

TABLE 3.—*Evaluation of Results*

Clinical Diagnosis	No. of Cases	Good	Fair	Poor
Arteriosclerosis (including diabetics)	Group A—49	30	13	6
	Group B—66	41	13	12
Arterial embolism, aneurysm, or thrombosis	Group A—10	6	4	
	Group B— 5	1	3	1
Buerger's disease (thromboanglitis obliterans)	Group A—31	28	2	1
	Group B—10	7	2	1
Frostbite and causalgia	Group A—21	17	2	2
	Group B— 8	5	3	
Thrombophlebitis, chronic	Group A—23	8	11	4
	Group B—23	17	4	2
Varicose or chronic leg ulcer	Group A—11	10	1	
	Group B— 2	2	0	
Unclassified	Group A—14	6	8	
	Group B— 2	2	0	

The average duration of symptoms in Group B was 50 months; the shortest was two months, and the longest, 10 years. In 90% of the patients the major and chief complaint was pain. In association with this, the frequency of ulceration, cellulitis, edema, and diminished or absent peripheral pulse was about the same frequency as in Group A (Table 2).

The postoperative evaluation indicated that the results were considered good to fair in about the same percentages in both groups, with a 90% excellent to good in Group A as against a 70% in Group B (Table 3).

Thrombophlebitis, Chronic.—In this category in both groups the number of patients were equal, being 23 upon whom, in Group A, 29 sympathectomies were performed (4 on the right, 13 on the left, and 6 were bilateral), whereas in Group B 9 were on the right, 6 were on the left, and 8 were bilateral.

The youngest patient was 29 years and the oldest, 71 years old, with the greatest number in the 31- to 40-year age groups in Group A (Table 1). The average duration of symptoms was 30 months; the shortest was 1 week, and the longest, 10 years. In 18 (78%) patients the major and chief complaint was pain. In association with this, 17 had edema, 3 had ulceration of the leg, and 1 patient had gangrene of the toe and another, of the foot (Table 2). In 15 patients there was a diminished or absent peripheral arterial pulse.

In Group B the youngest patient was 29 years and the oldest was 68 years of age, with the greatest number in the 51- to 60-year age group (Table 1). The average duration of symptoms was 45 months; the shortest was 2 weeks, and the longest, 17 years. In 16 (68%) patients the major and chief complaint was pain. In association with this, 22 had edema, 12 had ulceration of the leg, and only 1 patient had gangrene of the toes. The peripheral pulse was absent or diminished in seven cases (Table 2).

The postoperative evaluation indicated that the results were good in 8 (35%), fair in 11 (47%), and poor in 4 (18%) in Group A. In this chronic disabling disease some improvement was noted in 82%. The poorer results occurred in the group of patients who required ligation of one of the major venous vessels, such as the inferior vena cava, common iliac, or femoral veins.

In Group B the evaluation revealed the results to be good in 17 (74%), fair in 4 (18%), and poor in 2 (8%). Therefore, in 92% some improvement was noted following sympathectomy.

In the remaining three categories, namely, frostbite and causalgia, varicose or chronic leg ulcer, and unclassified diseases, the results were about the same in comparative groups (Tables 1, 2, and 3).

Comment

It is noted that, with the average age increase in the male population entitled to treatment at this hospital, the number of patients in several of the categories, as noted in Table 1, has changed from our original report of Group A. The greatest increase was noted in the patients with arteriosclerotic vascular insufficiency. This group alone constituted more than 50% of the entire series in Group B. Along the same line, there were fewer cases of Buerger's disease than in the previous series, with a 11% drop in the admission incidence in this category. There was, however, a continued need for surgical intervention in the group of patients with a postphlebitic syndrome. The total number were equal in the two groups, indicating that this condition occurs with about the same frequency as in the past and produces symptoms and disabilities of sufficient degree to require for many a more definitive surgical program.

The greatest number of patients in Group B were in the age group of 51 to 70 years, whereas in Group A the age groups were 51 to 60 and 31 to 40 years. This upward swing was due to the over-all increase in the average age of Group B and, therefore, brought more patients into the age groups when arteriosclerosis has its highest incidence.

As a result of this compartive study it is apparent that lumbar sympathectomy is being performed with about the same frequency as in the past on our services and that its indications on our services have remained unchanged since the inception of this program in 1946. Since the completion of this survey it appears, to date, that this procedure is being performed more frequently.

In the over-all evaluation of both groups the results were considered fair to good in 92% of the cases in Group A, as compared with 84% in Group B. However, in the largest group of patients in both series, arteriosclerosis, the over-all results were favorable in 66% of Group B as compared with 60% in Group A.

Those patients requiring amputation because of gangrene and associated changes were, in most instances, patients with peripheral arteriosclerosis. A greater number of amputations were performed below the knee in the latter group, being 70% as compared with 60%. However, in the entire series there was an increase of 6% in Group B requiring amputation, with an incidence of 9% in Group A. Generally speaking, the above-knee amputations were necessary because of the extent and progressive level of the gangrene. However, in all the remaining cases where the gangrene remained localized to the toes or to portions of the foot, a more conservative type of amputation was accomplished. This policy was also effective in the diabetic patients with arteriosclerosis.

Age alone was not considered a sole determining factor in the selection of patients for sympathectomy. As seen in this combined analysis, 30% of the patients were more than 60 years of age; nine patients were more than 70 years old. Favorable results will follow a sympathectomy if vasospasm exists and there is evidence of elastic potentialities in the unaffected vascular bed and smaller vascular channels.

Summary

The effects of lumbar sympathectomy in the treatment of a variety of peripheral vascular diseases in two groups of male patients upon whom operations were performed are presented. In Group A there were 159 patients upon whom 221 operations were performed from October, 1946, to December, 1951, as compared with 116 patients in Group B upon whom 170 operations were performed from January, 1952, to December, 1955. These studies included the following diseases or conditions: arteriosclerosis (including diabetics); arterial embolism, aneurysm, or thrombosis; Buerger's disease; frostbite and causalgia; chronic thrombophlebitis; varicose or chronic leg ulcer, and other conditions causing vascular insufficiency of undertermined causes.

The patients ranged from 20 to 85 years of age, with 30% of the patients more than 60 years of age.

The over-all favorable results in the two groups were almost equal, being considered fair to good in 88% of the cases. These favorable results were based upon improvement of circulation of the extremity due to release of vasospasm and the development of smaller collateral channels of the vascular bed not involved by the disease process.

Lumbar sympathectomy continues to be a valuable method of therapy for many diseases and conditions enumerated in this study; it carries a minimal risk and complication rate. It provides in properly selected cases early improvement or relief of symptoms, a more rapid healing of ulcers, diminution in peripheral edema, subsidence of cellulitis, and a dry extremity. The latter factor reduces the hazard of tissue maceration, subsequent bacterial and fungus infections. It may prevent or delay the need for a major amputation in some cases, with the result that many limbs which by former standards or methods of treatment would have been sacrificed were saved. If amputation becomes necessary, frequently it can be performed at a lower level with safety, and rapid healing can be expected in the majority of cases. In the combined series 68% of amputations, major and minor, were performed below the knee.

This method of management has resulted in earlier rehabilitation of many patients and has reduced their period of hospitalization considerably.

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Effect of Levallorphan Tartrate on Levorphanol Tartrate Analgesia in Postoperative Patients

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After major thoracic surgery it is important to provide efficient analgesia without the hazard of respiratory despression. In 1952 Fromherz and Pellmont [1] suggested, on the basis of animal experiments, that there may exist a ratio at which the respiratory depression induced by levorphan tartrate (Levo-Dromoran Tartrate)* could be counteracted by levallorphan tartrate (Lorfan Tartrate)† without significant loss of analgesia. Support for this theory was provided by Gross and Hamilton.[2] In normal human volunteers they found that on simultaneous administration less levallorphan tartrate was required to prevent respiratory depression than was necessary to affect the analgesia produced by levorphan tartrate. Cullen and Santos [3] reported favorably on a combination of 10 parts of levorphan tartrate and 1 part of levallorphan tartrate in patients with chronic pain. The present study represents an attempt to evaluate this combination in patients after major thoracic surgery. The aim of the study was to determine whether this combination could maintain satisfactory analgesia without respiratory depression and whether it was materially better than levorphan tartrate.

Method

The clinical material consisted of consecutive adult patients undergoing pulmonary resection for pulmonary tuberculosis. The series included both men and women. No observations were made on the day of operation. The data presented represent observations made on the first or second postoperative days only.

Levorphan tartrate or a mixture of 10 parts of levorphan tartrate to 1 part of levallorphan tartrate‡ was administered alternately whenever an analgetic was necessary. The patient therefore served as his own control. The identity of the drugs administered was unknown to the personnel evaluating the results, the vials being labelled A or B and the symbols being switched occasionally. The drugs were prepared in aqueous solution and administered subcutaneously. The dose of levorphan tartrate was similar, whether given alone or combined with levallorphan tartrate. All other analgetics or narcotics were stopped. Otherwise the routine postoperative procedure was followed.

The pulse and respiratory rates were noted at the time of administration and thereafter at intervals of 30 or 60 minutes for 6 hours. The patient's estimate of the severity of pain was graded: 0—no pain; 1—mild pain (admits to having pain but does not complain); 2—moderate pain (complains of pain), and 3—severe pain. This formed a basis for estimation of the effectiveness of analgesia. The duration of analgesia was noted as the time from administration until the patient asked for another injection. Control depression was graded: 0—no depression; 1—drowsy; 2—very drowsy or sleeping but responding to slight stimulation, and 3—roused only by considerable stimulation. Any undesirable side-effects were noted.

Group 1.—Seventy-six doses of levorphan tartrate, 2 mg. each, and seventy-two doses of levorphan tartrate, 2 mg., with levallorphan tartrate, 0.2 mg., were given in alternate doses to 27 consecutive postoperative patients.

Group 2.—A dose of levorphan tartrate, 4-5 mg., was compared with a similar dose combined with levallorphan tartrate, 0.4-0.5 mg, in 50 postoperative patients. Since doses of this magnitude usually produced analgesia which lasted most of the day, observations had to be made on two different days. As it was likely that pain would be less severe on the second day, the order of

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* Levorphanol tartrate (levo 3-hydroxy-N-methylmorphinan tartrate); formerly designated Levorphan tartrate.

† Levallorphan tartrate (levo 3-hydroxy-N-allylmorphinan tartrate).

‡ Provided for this study by Dr. M. J. Schiffrin, Hoffman-LaRoche, Inc.

TABLE 1.—*Average Change in Respiratory Rate from Control Values*
(Breaths per Minute)

	Hour After Injection	½	1	1½	2	2½	3	3½	4	5	6
Group 1	Levorphan tartrate, 2 mg.		−2.6		−3.6		−3.8		−3.0	−2.4	−3.6
	Levorphan tartrate, 2 mg. Levallorphan tartrate, 0.2 mg.		−2.2		−2.4		−2.1		−2.0	−2.2	−1.1
Group 2	Levorphan tartrate, 4 or 5 mg.	−2.9	−3.8	−3.5	−3.8	−3.9	−4.1	−4.4	−4.0	−3.6	−2.8
	Levorphan tartrate, 4 or 5 mg. Levallorphan tartrate, 0.4 or 0.5 mg.	−1.0	−3.0	−3.1	−3.2	−3.4	−3.6	−3.6	−3.4	−3.5	−2.4

administration was arranged so that an equal proportion of the patients received the combined mixture on the first or second postoperative days.

Results

Group 1 (2 mg. of levorphan tartrate).—The average preinjection pain estimate was 2.03 for levorphan tartrate and 2.07 for the combined mixture. It is probably reasonable to conclude, therefore, that variations found in any of the observations were not due to differences in the severity of pain at the time of injection. The addition of levallorphan tartrate produced little change, and the observers were unable to tell when it had been added. There were, however, differences in average values for the whole group.

The average maximum depression of respiratory rate from the control value was 9.92 for levorphan tartrate and 9.07 for the mixture. This occurred during the third hour. The average depression of respiration was slightly less with the mixture (Table 1). The pulse rate was not different in the two groups. There appeared to be a slight decrease in analgesia when levallorphan tartrate was added (Table 2). Cortical depression was slight and did not seem to have been influenced by the addition of levallorphan tartrate (Table 3). Approximately half of the doses produced drowsiness. Unpleasant side-effects were minimal.

Group 2 (4 or 5 mg. of levorphan tartrate).—With larger doses the results were very similar. The average preinjection pain estimate was 1.86 for levorphan tartrate and 1.79 for the mixture. The average decrease in respiratory rate from the control value was once again less when levallorphan tartrate was added (Table 1). Clinically this difference did not seem to be significant except at the first half hour after injection, when 18% of the patients receiving levorphan tartrate alone had a decrease of respiratory rate of more than 4 per minute, while only 8% of those receiving the mixture had a similar decrease.

The average duration of analgesia was 10.1 hours with levorphan tartrate and 10.2 hours with the mixture. Distribution curves of the duration of analgesia were similar. A summary of these is seen in (Table 4). The addition of levallorphan tartrate, therefore, had not produced any significant difference in the duration of analgesia. Once again, however, analgetic efficiency seemed to be slightly less with the combination (Table 2). In the first six hours after injection slight or no pain was noted in 94.5% of the observations after levorphan tartrate and in 89% of the observations after the combined drugs. The necessity of using the patient as his own control when assessing subjective symptoms is demonstrated by the fact that otherwise one might conclude that 2 mg. of levorphan tartrate was more effective than 4 mg. (Table 2).

TABLE 2.—*Percentage of Patients with Complete Analgesia*

	Hour After Injection	½	1	1½	2	2½	3	3½	4	5	6
Group 1	Levorphan tartrate 2 mg.		80		84.2		75		71.5	64	49.5
	Levorphan tartrate, 2 mg. Levallorphan tartrate, 0.2 mg.		74		72.4		68.8		67	59	28
Group 2	Levorphan tartrate, 4 or 5 mg.	58	76	82	80	82	82	82	74	64	48
	Levorphan tartrate, 4 or 5 mg. Levallorphan tartrate, 0.4 or 0.5 mg.	58	62	72	70	70	70	66	60	58	48

TABLE 3.—*Depression of Cerebral Cortex*
(Percentage of Patients)

	0	1	2	3
Group 1				
Levorphan tartrate, 2 mg.	41	20	39	0
Levorphan tartrate, 2 mg. / Levallorphan tartrate, 0.2 mg.	45	14	41	0
Group 2				
Levorphan tartrate, 4 or 5 mg.	2	30	58	10
Levorphan tartrate, 4 or 5 mg. / Levallorphan tartrate, 0.4 or 0.5 mg.	0	34	60	6

0—No depression of consciousness
1—Drowsy
2—Very drowsy; roused by slight stimulation
3—Roused only by considerable stimulation

Unpleasant, but rarely serious, side-effects were common with these large doses. Some degree of depression of cortical activity was present in 98% of the patients (Table 3) but, even where it was most marked, was not sufficient to cause concern. Levallorphan tartrate did not influence the degree of cortical depression to any significant extent. Unpleasant pruritus, mainly of the face and hands, giddiness, and severe apprehension occurred with the same frequency, but nausea and vomiting were more frequent after the combined drugs (Table 5). In addition, one patient developed frightening hallucinations, and another became confused and disoriented.

TABLE 4.—*Duration of Analgesia*
(Percentage of Patients)

	Levorphan Tartrate, 4 or 5 mg.	Levorphan Tartrate, 4 or 5 mg. Levallorphan Tartrate, 0.4 or 0.5 mg.
8 hr. or less	40	36
9-12 hr.	44	48
13-16 hr.	12	10
17-20 hr.	4	6

TABLE 5.—*Toxic Effects*
(Percentage of Patients)

	Lavorphan Tartrate, 4 or 5 mg.	Levorphan Tartrate, 4 or 5 mg. Levallorphan Tartrate, 0.4 or 0.5 mg.
Nausea	22	36
Vomiting	8	18
Dizziness	8	10
Pruritus	10	10
Apprehension	8	8

Comment

The ability of levallorphan tartrate to antagonize the respiratory depressant effects of levorphan tartrate has been amply demonstrated both in animals [1,4,6] and in man.[2,5] Considerable evidence is forthcoming to support the contention that, in a combination of appropriate ratio, efficient analgesia can be obtained without respiratory depression.

In animals at ratios of 1:1 to 1:5 levallorphan tartrate completely antagonizes [1,4] levorphan tartrate analgesia, while at ratios of 1:8 to 1:20 respiratory depression is abolished but analgesia is only partly decreased.[1,6]

The results in man have been similar. Utilizing the Wolff-Hardy-Goodell technique, Gross and Hamilton [2] demonstrated that in normal human volunteers 0.05 to 0.5 mg. of levallorphan tartrate did not interfere with the analgesia produced by 1 mg. of levorphan tartrate. Cullen and Santos,[3,7] however, reported that a ratio of 1:4 resulted in a loss of analgesia and an increase in unpleasant side-effects, while a ratio of 1:8 to 1:10 resulted in no loss of analgesia and a decrease in respiratory depression in patients with acute or chronic pain. In postoperative patients [7] these investigators are of the opinion that a 1:10 combination produces a more marked sedative action and an analgetic effect of longer duration than would have been achieved with levorphan tartrate alone.

In the present series the differences were not striking. No differences in sedative effect were noted. The slight reduction in respiratory depression and analgesic efficiency lack conclusive statistical significance and appeared to be of doubtful clinical significance.

Levorphan tartrate when used alone is a very efficient analgetic which is remarkably free of serious side-effects when administered to patients in severe pain. Even in doses of 4-5 mg. (which are not recommended routinely), no serious depression of respiration was noted in this group of

postoperative thoracic patients. The value of levallorphan tartrate in combating any respiratory depression which may arise is beyond question, but the routine addition of 1 part of levallorphan tartrate to 10 parts of levorphan tartrate in the present series seemed to be without clinically significant benefit, and at the same time there was the suggestion that the incidence of nausea and vomiting was increased. Although perhaps of value in other circumstances, we feel that further study is required and that, until more conclusive proof is forthcoming, levallorphan tartrate should be reserved for the treatment of opiate-induced respiratory depression.

Summary

An attempt to compare the effect of levorphan tartrate, used alone or in combination with levallorphan tartrate for relief of pain after major thoracic surgery, is described. The slight decrease in respiratory depression and analgesia produced by the addition of levallorphan tartrate is probably not clinically significant, and at the same time the incidence of nausea and vomiting appears to be increased. The use of levallorphan tartrate should be reserved for the treatment of respiratory depression when it occurs after the administration of opiates.

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Incorporation of P^{32} into Mouse Mammary Cancer

Influence of Estrogen and Testosterone

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Introduction

The effect of estrogens and androgens on some neoplasms of the human reproductive system, though unpredictable, has been sufficiently dramatic to warrant continued investigation. The growth rate of mammary carcinoma in particular appears to be subject to modification by these hormones in a substantial number of cases. The mechanism of action, however, is unknown. Strains of mice developing spontaneous mammary cancer in a high proportion of the females offer an appropriate laboratory preparation for the study of basic growth mechanisms involved. These tumors can be readily grafted into males of the same strain. Endogenous estrogen or androgen production can be reduced by castration in both sexes, and the influence of exogenous hormone on basic biochemical alterations is then more clearly defined. We have chosen to study the effect of 17β-estradiol and testosterone propionate on incorporation of P^{32} into the total nucleic acids of these tumors. In a previous study [1] both male and female mice bearing transplanted mammary tumors were injected for three days with either estrogen or androgen before being killed, and samples of the tumor were then incubated with radioactive phosphorus. It was reported that estrogen caused an increase of P^{32} incorporation into the nucleic acids of mammary carcinoma in castrated females, while testosterone appeared to produce a greater incorporation into grafted tumors in males. In the present investigation P^{32} was employed in vivo as well as the steroids before killing. The results confirm the previous work. The steroids used apparently caused a modification of the amount of P^{32} incorporated into the tumor nucleic acids, and the character of the change produced appeared to be dependent primarily on the sex of the host animal harboring the tumor.

Material and Methods

C_3H female mice bearing spontaneous mammary Adenocarcinoma H2712J were obtained from the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Me. These animals were found to be too old or cachectic for direct application to the study but were used as "donors." Six-week-old C_3H mice of both sexes weighing 22-30 gm. were also obtained and, after one week of acclimatization, were castrated to eliminate gonadal steroid production. Three days after castration the animals were anesthetized, and approximately a 2 cu. mm. fresh piece from a "donor" tumor was inserted through a small incision subcutaneously in the inguinal region. An effort was made to use the same size of implant in each case. The donor tumors varied in size from 1.5 to 4 cm. in diameter. In each test run, a single donor was used for grafting all the animals used that day. The transplants were usually palpable by the 4th or the 5th day after grafting, and a rapid increase in growth took place on the 8th, 9th, and 10th days. The largest transplant measured more than 3 cm. in greatest diameter on the 10th day in a preliminary study of untreated controls. At that time such animals generally showed systemic effects of this growth by decreased activity and changes in the quality of their fur. We therefore arbitrarily

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TABLE 1.—*Effect of Estrogen and Testosterone on Specific Activity of Nucleic Acid P in Tumor Transplants*

Exp. No.	No. of Mice	No. of* Flasks	Specific Activity†				
			Control	Estrogen	Control, per Cent	Testosterone	Control, per Cent
Females							
I	18	24	322± 38.8	309± 20.6	96	185±13.5	57
III	18	18	884± 56.9	1044± 22.0	118	653±72.3	74
IV	18	18	982±134.6	1427±173.6	145	700±27.5	71
VI	18	18	925± 19.3	1118± 30.8	121	744±65.5	80
IX	18	18	369± 12.1	470± 23.4	127	361±15.3	98
Males							
II	18	18	168± 18.1	119± 9.9	71	236±18.7	140
V	18	18	288± 20.0	232± 9.7	81	346±23.4	120
VII	18	18	830± 49.9	620± 68.5	75	1236±84.1	149
VIII	18	18	365± 6.0	349± 8.8	96	397±15.1	109

* Eight samples from each tumor pool were used in Experiment I; six samples in all others.
† Mean specific activity in counts per minute per milligram of nucleic acid phosphorus ± standard error.

chose Day 4 after grafting as the optimum time to initiate steroid treatment when the mice were still healthy and vigorous. Injections were given into alternate thighs on Days 4, 5, and 6 after grafting, and necropsies were performed on Day 7, ten days after castration. Both sexes received the same daily dose of steroid—2γ of estradiol dipropionate, or 2γ of testosterone propionate[3] in 0.2 ml. of sesame oil, and the controls received this amount of oil only for three days. On the day of the last injection all animals were given 20μc of P^{32} in 0.5 ml. of saline intraperitoneally through a No. 26 gauge needle. Exactly 24 hours after this last injection they were killed. The healthy tumor tissue from the several animals in any one group—experimental or control—was then pooled and minced on ice. These separate tissue pools were washed with 4 vol. of cold 7% trichloroacetic acid and then homogenized in 10 to 20 vol. of the same solution. The phospholipids were removed by washing with 3:1 ethanol-ether, and the residue extracted twice with 5% trichloroacetic acid at 90 C for 15 minutes to yield the total nucleic acid fraction. After this extraction, aliquots of the supernatant fluid from each tissue pool were decanted into six test tubes and analyzed for phosphorus according to the method of Fiske and Subbarow,[4] following digestion with hot sulfuric acid and hydrogen peroxide. Other aliquots of the same supernatant from each tissue pool were counted in duplicate for radioactivity with use of an end-window Geiger counter with appropriate corrections for absorption, background, and coincidence.[2] The specific activity (S. A.) for the total nucleic acid phosphorus is expressed as counts per minute per milligram of phosphorus.

Results

Eighteen animals of the same sex were used in each of the nine experiments; six received sesame oil only as controls, six were treated with estrogen, and six with testosterone. The mean specific activities ± standard error for the three groups in each experiment and the ratio of the treated group to the controls expressed as a per cent are recorded in Table 1. Since the standard errors are unequal but correlate with the numerical value of the means, a logarithmic transformation of the counts was used for statistical evaluation. The logarithmic means are shown in Table 2. An analysis of the variation associated with the different days of experimentation, the treatments, and the different aliquots of each tumor pool is summarized in Table 3.

TABLE 2.—*Conversion of Specific Activities to Means of Log Counts*

	Exp. No.	Control	Estrogen	Testosterone	Standard Error of a Treatment Mean	
Females	I	2.4875	2.4828	2.2586		
	III	2.9416	3.0184	2.8026		
	IV	2.9616	3.1376	2.8432		
	VI	2.9658	3.0462	2.8629		
	IX	2.5663	2.6092	2.5555	In any 1 Exp.*	0.05199
	All	2.7660	2.8466	2.6392	In toto	0.02252
Males	II	2.2119	2.0676	2.3631		
	V	2.4536	2.3638	2.5338		
	VII	2.9145	2.7788	3.0676		
	VIII	2.5620	2.5424	2.5972	In any 1 Exp.	0.05992
	All	2.5355	2.4382	2.6464	In toto	0.02596

*Except Experiment I in which eight rather than six aliquots were used for each treatment group.

TABLE 3.—*Analysis of Variance on Log Counts*

	Source	D.F.	Mean Square	F(Variance Ratio)	P-Value
Females	Days	4	1.36606		
	Treatment	2	0.34973	21.56	$P<0.001$
	Day×treatment	8	0.01622		
	Between aliquots	81	0.00876		
Males	Days	3	1.58785		
	Treatment	22	0.25806	11.98	$P<0.01$
	Day×treatment	6	0.02154		
	Between aliquots	60	0.00602		

Error term utilized in each case was Day×Treatment mean square.

The over-all differences between treatments were significantly greater in each sex than the variation among treatment means from day to day (Day × Treatment interaction term). The geometric treatment means and the 95% interval estimates are given in Table 4.

Tumors in castrated females treated with estrogen showed a 20% increase of P^{32} incorporation into the nucleic acid fraction when compared with the controls (Table 4), and a 25% decrease of this incorporation when treated with testosterone. These changes are statistically significant.

A reverse trend was recorded in tumors transplanted into castrated males. Estrogen gave a decrease to 80% of the controls, but testosterone increased P^{32} incorporation into tumor nucleic acids by 29% (Table 4).

In a further summary of these data the effects of the hormones in males were contrasted with the effects in females. The differences between the effects of both estrogen and testosterone in each of the two sexes was highly significant (Table 5).

Comment

In rat uterine deciduomata a close correlation has been noted between growth increments and uptake of P^{32} over the course of six days.[5] We do not have data in the present study to confirm changes in rate of incorporation. Our results tend to suggest, however, that estrogen stimulates the growth of this mammary tumor in the female, while testosterone induces increased growth of transplants of the same tumor in the male. This conclusion is challenged by the results of somewhat similar studies by Davidson and Freeman.[2,3] These authors demonstrated that the rate of P^{32} incorporation into nucleic acids of Adenocarcinoma 775 in a different strain of mice did not correlate well with tumor growth inhibition produced by a large number of antitumor compounds. This inhibition of growth was determined in a relatively chronic experiment started one day after transplantation of the tumor and continued for three weeks.[6] Since inhibition was based on weight of excised, treated tumors compared with controls, only gross differences could be detected. In the present study gross wet weights of excised tumors were recorded, before dissecting healthy from unhealthy tissue, and showed the same trend indicated by the P^{32} uptake studies. Tumors in the females treated with estrogen and in the males treated with testosterone, in general, totaled considerably more in gross weight than in the controls. Varying degrees of necrosis and hemorrhage, fatty infiltration

TABLE 4.—*Statistical Analysis of Results (Geometric Means)*

	Control	Estrogen	Testosterone
Females			
Mean	583.5	702.4	435.7
Range (95% limits)	518–658	623–792	387–491
Mean, per cent of controls		120%	75%
Range (95% limits)		102%–142%	63%–88%
P-value		<0.05	<0.01
Males			
Mean	343.0	274.3	442.0
Range (95% limits)	290–405	232–325	373–523
Mean, per cent of controls		80%	129%
Range (95% limits)		63%–101%	101%–164%
P-value		>0.05	<0.05

TABLE 5.—*Comparison of Hormone Effect in Females and Males*
Log Values

	Estrogen minus Control	Testosterone minus Control
Female	+0.0806	−0.1268
Male	−0.0973	+0.1099
Difference (female−male)	+0.1779	−0.2367
Standard error of difference	0.052	0.052
t-value	3.421	4.552
P-value	<0.01	<0.01

and fibrosis, however, render such figures in our opinion not worth recording.

No clear explanation is apparent for the contrasting effects of these sex steroids on the same tumor transplants in male and female hosts. An interval of seven days after castration elapsed before starting the three-day program of hormone injections. The uteri of the control, uninjected females were atrophic on Day 10 at time of autopsy. It was felt that such an interval of time should be sufficient to allow for base-line castration effect in both sexes upon which to superimpose the selected hormonal environment by appropriate injections. The clear-cut contrast in response between grafted tumors in male and female hosts leads to the postulate that the total hormonal environment bathing the tumors differed according to the sex of the grafted animal. Whether or not this is associated with a contrast in endocrine response to castration between the sexes or to some genetic factor is purely conjectural.

Summary

Estrogen and testosterone were tested for their ability to modify the incorporation of P^{32} into the total nucleic acids of mouse mammary Adenocarcinoma—H2712J transplants in both male and female castrated C_3H mice. The results showed a clear-cut contrast related to the sex of the grafted animal. Estrogen significantly increased the uptake of P^{32} into tumors grafted into females, while testosterone depressed this activity. In tumor transplants harbored by male animals, however, the exact reverse was recorded. It is suggested that this tumor is sensitive to these particular steroids, and the effect is mediated in some way not clearly defined by the sex of the host prior to castration.

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Dr. Mindel C. Sheps, of the Department of Preventive Medicine, Harvard Medical School, supervised and interpreted the statistical analysis of the results, and Miss Rita Nickerson performed the necessary computations. The steroids used in this study were supplied by the Ciba Pharmaceutical Products, Inc.; in addition to supplying isotopes Dr. A. K. Solomon, of the Harvard Biophysics Laboratory, Harvard Medical School, assisted in evaluating tissue radioactivity.

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Dioctyl Sodium Sulfosuccinate (Colace) Following Proctologic Operations

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Introduction

The proctologic aspects of constipation were presented from a broad biologic standpoint at a symposium on the normal and abnormal physiology and therapeutics of the colon held by the Section of Biology of the New York Academy of Sciences on May 8 and 9, 1953.[1] Lesions such as diverticulitis, complete and incomplete colonic obstruction, megacolon and other congenital colonic and anorectal malformations, anal fissure, so-called "pectinosis," hemorrhoids, prolapse, and megarectum were discussed briefly. It was then stated that "laxatives have no place in the therapy of constipation caused by organic etiologic factors." Although functional constipation, or constipation on a habit basis, hardly belongs in the realm of the proctologist, I nevertheless stated that with Ogilvie I believe that "in the absence of organic causes, normal defecation usually 'comes from equanimity and common sense.' Hardly ever do I find a need for cathartic drugs in the management of the noninstitutionalized cooperative patient afflicted by constipation from any cause." These statements are as valid today as they were when first pronounced.

Background Data

In 1940, fifty patients of varying ages (30 to past 70 years old) who had undergone anorectal operations, notably hemorrhoidectomy (29 cases), were observed for 72 hours postoperatively to determine the incidence of spontaneous bowel evacuation. These patients received narcotic and sedative drugs for the control of postsurgical pain and were ambulated within 12 to 24 hours. They received a soft diet with fluids as tolerated the day of the operation and were given a regular hospital diet with a normal fluid intake thereafter. A digital rectal examination was made on the third postoperative day for the detection of fecal accumulation in the ampulla. Also, 10 of the very cooperative patients were instructed to drink an abundance of fluids (eight or more glasses of water, fruit juices, coffee, or tea) in addition to their regular daily fluid intake.

Of the 50 patients, 13 had spontaneous bowel movements between 48 and 72 hours. Six of these registered considerable pain, owing to the passage of what they described as "hard" stools. Of the remaining 37 patients, 30 required a cathartic after 72 hours, while 7 received oil retention enemas in an effort to relieve fecal accumulation in the ampulla. Most of these patients had pain of variable degrees after the first bowel movement; more than 50% of these patients required coal-tar derivatives for the relief of pain. The 10 patients who drank an extra amount of fluids did not fare differently from the other 40 patients. This shows that excessive ingestion of fluids has hardly any special virtue or influence on bowel movements or on the character or bulk of the patients' stools following the performance of anorectal operations. This is in agreement with Ingelfinger's[2] more recent and better controlled experimental studies.

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Most of this material forms the basis for an exhibit that will be shown at the Annual Meeting of the American Medical Association to be held in New York in June, 1957.

As a result of the foregoing study, I began to prescribe liquid petrolatum almost routinely for all patients undergoing anorectal operations beginning on the first postoperative day. In addition to liquid petrolatum, a laxative was prescribed 72 hours after operation for patients whose bowels failed to act by that time. This program was continued until recently.

Liquid petrolatum was prescribed with a view to preventing the formation of hard stools and thus reducing pain following the initial bowel movement.

The liquid petrolatum was administered in a dose of about 30 cc. daily, taken two hours before or two hours after a meal, and was continued for about 5 to 30 days. In an experience with more than 2000 clinic and private patients, except for one case of suspected lipid granuloma of the lungs, I have neither observed any of the alleged deleterious systemic effects nor noted interference with the effective healing of the wounds even in the presence of oily leaks, as claimed by some authors. I have, however, always limited the intake of liquid petrolatum to the barest minimum and for the shortest possible duration because of (1) the known hazards of aspiration, resulting in the development of lipid pneumonitis; (2) the objections by the very fastidious patients to infrequent oily leaks which interfere with their standards of anal hygiene, and (3) the potentially irritating effect upon the anal canal by the oil. This irritation is believed to be augmented by the liquid stool that is invariably produced by liquid petrolatum. These liquid, bacteria-laden feces may lodge in the anal crypts and set up inflammatory or suppurative processes in these and other preformed anal structures.

The recent studies on the positive correlation between cancer of the alimentary tract and the ingestion of liquid petrolatum cannot be ignored.[6]

Recently, dioctyl sodium sulfosuccinate U. S. P. (bis[2-ethylhexyl] sodium sulfosuccinate [Colace]) has become commercially available. According to the report released by the Council on Pharmacy and Chemistry, of the American Medical Association, this substance is relatively inert pharmacologically when given by mouth but lowers surface tension in the alimentary tract. Its action is similar to that of a detergent. It appears to allow water and fatty material to penetrate and thus be better mixed with the feces, invariably resulting in a softer but homogeneous formed stool of normal bulk. At the date of this writing, no irritation in the colon or rectum has been observed following the administration of therapeutic dosages of this compound. In clinical practice, 200 mg. to 300 mg. is given initially for two to four days to adults in two divided daily doses, followed by a daily maintenance dose of 50 mg. to 100 mg. Larger doses have been administered without untoward effects, showing the toxicity of this compound to be negligible. Its effect on the absorption of fats or fat-soluble vitamins in normal persons is also apparently nil unless it is administered with liquid petrolatum, whose absorption it may enhance.

Present Investigation

The following is a clinical investigation of the value of the recently introduced dioctyl sodium sulfosuccinate following the performance of proctologic operations and the disposition of adenomas by means of electrothermia.[4]

To date, dioctyl sodium sulfosuccinate has been used in 105 patients following excision of anal fissures (32 cases), after anal fistulectomies (7 cases), following hemorrhoidectomies (60 cases), and after miscellaneous operations (6 cases). The patients ranged in age from 27 to 74 years. The administration of this compound may be started either 12 hours before operation or 36 hours before admission to the hospital. However, it is usually begun 6 to 12 hours after the conclusion of the operative procedure or just as soon as the patient begins to drink fluids liberally.

In the first 20 patients, 200 mg. (in two divided doses in the form of 50 mg. capsules) was administered with a full glass of water every 12 hours, starting within 12 to 24 hours after operation. Sixteen patients had a soft but formed stool of normal bulk within 48 to 72 hours. The pain following the first bowel movement was described as mild by 10, moderate by 4, and moderately severe by 2 of the patients. The pain was easily controlled by hot sitz baths; narcotic drugs were not required. Of the remaining four patients, three had prompt bowel movements following the administration of a laxative. Their ages were 59, 67, and 74 years, respectively, and they had been profoundly habituated to cathartics for many years. The fourth patient, a woman 62 years of age, was given a saline enema because of fecal accumulation in the ampulla. She greately feared postdefecatory pain, because she had experienced severe pain some 20 years ago after a hemorrhoidectomy which was performed elsewhere by means of electrothermia. In the older age group, 22 other patients, most of whom were habituated to cathartics, required stimulation of the bowel in addition to dioctyl sodium sulfosuccinate. Of these patients, three of four, following the administration of one dose of a cathartic, continued to have daily bowel movements while they remained on a maintenance dose of 100 to 200 mg. of dioctyl sodium sulfosuccinate. The fourth patient required periodic stimulation by means of cathartics in addition to the use of the detergent.

For the remaining 63 patients, whose ages varied from 34 to 51 years, the dose of dioctyl sodium sulfosuccinate was increased from 200 mg. to 300 mg. (given in two or three divided doses). Of these patients, 55 had bowel movements within 48 to 72 hours, after which they were discharged from the hospital to resume more or less their preoperative mode of living. Included in this group were several patients who initially feared the first bowel movement but who, after a short interview, had bowel movements without incident. The need for continuation of dioctyl sodium sulfosuccinate was established on the individual merits of each patient. In this group of patients, dioctyl sodium sulfosuccinate had successfully replaced liquid petrolatum. In three of the remaining eight patients, the stools failed to liquefy in spite of the administration of 400 to 600 mg. of dioctyl sodium sulfosuccinate given in two divided doses. This occurred during the hot weather when these patients perspired freely. The fourth patient developed diarrhea, beginning 36 hours after the institution of dioctyl sodium sulfosuccinate or after a total of only 300 mg. to 400 mg. had been administered. Diarrhea also occurred in a woman four months pregnant and subsided after discontinuation of the medication. The sixth patient would neither swallow all the capsules nor take this compound in solution primarily because of the bitter taste. In two other patients there was an accumulation of soft stools in the ampulla some 72 hours after operation, which were easily removed by means of flushing saline edema to which 10 cc. of 1% solution of dioctyl sodium sulfosuccinate was added to each liter of normal solution.

The problem of pain at or following the first postoperative bowel movement paralleled that of the first 20 patients in the pilot group.

The wounds of 104 patients healed without incident.

Dioctyl sodium sulfosuccinate, instead of liquid petrolatum, was also administered routinely to more than 30 patients after disposition of adenomas in the office or hospital by means of electrothermia, with results paralleling those following proctologic operations.

Dioctyl sodium sulfosuccinate has been used successfully postoperatively in four patients after excision of pilonidal cysts and sinuses and in eight patients after extensive unroofing of pilonidal abscesses. Their ages varied from 18 to 33 years.

In seven patients with sigmoid colostomies after abdominoperineal resection of the rectum following the oral administration of doses varying from 200 to 400 mg. of dioctyl sodium sulfosuccinate, softening of feces occurred in five so that less time was required for effective irrigation. In the sixth patient the results were moderately good, while the seventh patient continued to form hard feces.

Parenthetically, it may be stated that dioctyl sodium sulfosuccinate solution in 1% or higher concentration is very effective for softening and eliminating established fecal impactions in surgical and nonsurgical cases. The recommended dose is 5 cc. in 60 to 90 cc. of water and is used as a retention enema for several hours. The retention enema is followed by a saline flushing enema or by one containing 5 cc. of the 1% solution of dioctyl sodium sulfosuccinate for each 500 cc. of the enema fluid. Thus used, this compound was successful in seven out of eight cases. The eighth could not retain the enema and required manual removal of the impacted feces under anesthesia.

Comment

With the cooperation of the referring clinician, I often utilize the immediate postoperative period for reeducation of the patient with constipation of fact or conviction. The program consists mainly of reassurance, an adequate and nutritionally well-balanced diet, and regularity of meals and habit times. More recently I have followed Almy's advice of feeding a large breakfast to promote a powerful gastrocolic reflex. In the past liquid petrolatum or plantago seed was utilized to some extent. Recently dioctyl sodium sulfosuccinate has been given a trial.[5] Laxatives are avoided; however, when a laxative has to be employed as a part of the bowel reeducation, I prescribe senna or cascara sagrada as a short-term treatment. Since I do not have an adequate long-range follow-up observation on most patients, it is impossible for me to evaluate any long-term results. In general, the success of this regimen depends on (1) the patient's age, (2) the patient's degree of habituation to cathartics, (3) the patient's educational level, (4) the patient's willingness to cooperate and to be helped, and (5) the patient's preconceived peculiar ideas about bowel habits and other phobias. The last-mentioned factors are extremely difficult to manage or to modify, let alone to eliminate. While under surveillance, most of these patients cooperated, but a number of them reverted to the old habit or custom immediately after termination of their medical contact. In general, prolonged and adequate follow-up is difficult to secure, as most patients, following successful or curative operations for benign proctologic lesions, are loath or downright unwilling to return for periodic observations. Incidentally, these patients are notorious for changing from physicians who attempt to change their lifetime bowel habits. A number of these patients appeared to be unstable and hypochondriac; some were clear-cut psychoneurotics who utilized constipation with its manifestations for psychological needs. Parenthetically, it has been stated that the human is the only animal interested in its excreta.

Summary

Many patients who undergo anorectal operations require an agent that will promote the smooth passage of stool of normal or near normal bulk at the first postoperative bowel action. Dioctyl sodium sulfosuccinate has proved to be a safe agent for this purpose, as well as following electrocoagulation of adenomas, and after surgical procedures for pilonidal disease. In my practice it is now standard procedure in place of conventional liquid petrolatum, which has been almost completely superseded. A stimulant laxative is required in addition to dioctyl sodium sulfosuccinate for some patients, mostly elderly persons, as well as for the preponderance of those patients who are

habituated to cathartics. Occasionally a flushing saline enema with or without dioctyl sodium sulfosuccinate solution is given for the expulsion of postoperative fecal accumulation in the ampulla.

The value of dioctyl sodium sulfosuccinate for the management of fecal impaction has also been mentioned. This compound is also receiving a trial in colostomized patients, particularly after abdominoperineal resection of the rectum (seven cases) as well as after resection and anastomosis of the colon.

25 E. 83d. St. (28)

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Evaluation of Peptic Ulcer Therapy Based on a Five- to Ten-Year Follow-Up Study

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In 1920 Dr. Leonard Rowntree was invited by Dr. W. J. Mayo to come to the Mayo Clinic as chief of medicine and director of clinical research. A research unit was set up where investigations in metabolic, renal, and hepatic diseases were carried out by Fitz, Wild, Amberg, Snell, Greene, and others. Rowntree suggested to Snell, Greene, and myself that we undertake a study of tests of liver function. It was these studies,[1] I believe, that led to a continuation by us of clinical investigations in diseases of the liver and their treatment, particularly those associated with obstructive jaundice. These collaborative studies between internist and surgeon led to better care for the patients and better results in treatment. Snell and I continued our association in the study of diseases of the liver, gall bladder, and bile ducts when we became members of the Mayo Clinic staff.[2]

These references are made only to illustrate the effect of Rowntree's influence in research medicine on three of the fellows of the Mayo Foundation, and we were only a few of those who received the benefit of his advice and encouragement in pursuing investigative studies in various fields of medicine. For example, it was he who brought George Brown to the clinic and suggested to him that the field of peripheral vascular disease would lend itself readily to study and investigation. Soon Brown had gathered around him some brilliant associates, including Allen and Barker, and they, in turn, trained Hines and Kvale. Their contributions to the field of peripheral vascular disease, I am sure, are known to all of you. Rowntree stimulated Adson to take up the work of Hunter and Royal in studying the effects of sympathectomy in the treatment of certain neuromuscular disturbances of the extremities and in the treatment of certain types of vascular hypertension. Hench's interest in rheumatic disease led to his investigation of the effects of various metabolic diseases on rheumatic pain and to the study by him and his associates, Slocumb and Polley,[3] of the use of the steroids of the adrenal cortex, isolated by Kendall,[4] which brought Nobel Prizes to both Hench and Kendall.

While working at Johns Hopkins Medical School, in the laboratory, Rowntree had discovered a compound, phenolsulfonphthalein, which, when injected into human beings, was excreted by the kidneys proportionately to their functional ability and hence became an important test of renal function. By experimenting with other halogenated phthaleins, he found that the dye sulfobromophthalein (Bromsulphalein) was excreted by the liver into the bile. From this discovery came the Rowntree-Rosenthal test for liver function. The retention of the dye in the blood, or the lack of retention, is a good indicator of liver function. This has continued to be one of our best single tests of liver function in the absence of jaundice. During his Hopkins days with Dr. Abel, Rowntree constructed the first artificial kidney, discovered the presence of amino acids

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Phi Beta Pi lecture at the University of Miami, Miami, Fla., Dec. 8, 1956, honoring Dr. Leonard Rowntree.

From the Section of Surgery, Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

in the blood, and laid the groundwork for transfusions with erythrocytes.

From Johns Hopkins Rowntree went to the University of Minnesota, where he was professor of medicine and chief of the department of internal medicine. From there he came to the Mayo Foundation, where he became chief of the department of medicine and director of clinical research. A member of the most important medical and research societies, he served with distinction in both World War I and World War II, in the latter as chief of the Medical Division of the Selective Service System, and was the recipient of the Presidential Medal for Merit. He was the chief medical adviser and chairman of the advisory board of the American Legion and, as such, was one of the first two to suggest to Generals Bradley and Hawley, of the Veterans' Administration, that the collaboration of the Veterans' Hospitals with the faculties of the university medical schools in the teaching and the practice of medicine and surgery would result in great benefit to patients in Veterans' Hospitals and to the teaching program afforded to the graduate resident medical students of the universities. This was the start of the Dean's Committees, which implemented the program.

Dr. Rowntree has continued his manifold interests in the field of scientific medicine in all its aspects. When he moved to Miami, he was one of the leaders in securing a medical school for the University of Miami. It is a great honor and a privilege to be invited to give the first Phi Beta Pi lecture of the University of Miami in his honor.

I wish to discuss this evening some of the results of different methods of treating chronic peptic ulcers, emphasizing the significant physiologic factors concerned and the objective which one hopes to obtain in their surgical treatment.

Physiologic Objectives of Present-Day Treatment of Peptic Ulcers

Present-day treatment of benign gastric and duodenal ulcer is directed toward reduction of gastric acidity and the relief of gastrospasm. Both of these objectives are obtained when the patient is given mental and physical rest away from his work, preferably in bed in a hospital. Under these conditions the effects of cerebral stimuli carried through the vagus to the stomach are decreased, gastric secretion is lessened, and gastric acidity is reduced. A soft, bland diet decreases gastric motility by making it unnecessary for the musculature of the stomach to work so hard to force the food through the pylorus and past a duodenal ulcer, if one is present, that produces partial obstruction by spasm, edema, and fibrosis. In addition to the previously mentioned methods of reducing cerebral stimulation of gastric acidity through the vagi, long-acting antispasmodics and sedatives are used, and intragastric control of gastric acidity is accomplished by frequent feedings, by the use of such antacids as aluminum hydroxide, and occasionally by such alkalies as sodium bicarbonate, magnesium oxide, and bismuth subcarbonate. The response to such a regimen is frequently dramatic when a crisis-like type of penetrating ulcer is present, but unfortunately the results are temporary in most cases, even though an ambulatory medical regimen is continued.

From a surgical standpoint these criteria for treatment are obtained by removal of a half to two-thirds of the stomach and that part of the duodenum containing the ulcer whenever it is possible and safe to do so, or by gastroenterostomy either with or without associated vagotomy.

Reflux of pancreatic, biliary, and duodenal secretion into the stomach through the gastrojejunal anastomosis, after gastroenterostomy or gastric resection performed for duodenal ulcer, plays an important role in reducing gastric acidity, in the healing of the duodenal ulcer, and in the prevention of recurring ulceration. This is evidenced further by the fact that when an enteroanastomosis is made between the two loops of jejunum attached to the stomach and the reflux of the secretions into the resected

stomach is prevented for the most part achlorhydria occurs in only about 40% of the patients undergoing a two-thirds partial gastrectomy instead of the 72% to 75% that have achlorhydria when enteroanastomosis is not performed. Furthermore, the incidence of recurring ulceration is much greater than when enteroanastomosis is not performed. In my opinion the reason for the greater frequency of ulceration after Billroth I (gastroduodenal) type of resection than after the Billroth II (gastrojejunal) type is that in the former the alkaline biliary, duodenal, and pancreatic secretions are carried away from the resected stomach, but in the latter these secretions are carried into the stomach.

When an adequate amount of stomach, including the ulcer, is removed in the course of partial gastrectomy for gastric ulcer, acidity decreases to achlorhydric levels almost without exception with both the Billroth I and the Billroth II operations, and recurring ulceration seldom occurs. But gastric ulcer is quite a different lesion from duodenal ulcer, not alone in the physiologic chemical factors involved in its formation but in its pathologic aspects and its response to surgical treatment.

Results of the Billroth I and Billroth II Resections

Although partial gastrectomy was uniformly accepted in this country as the preferable procedure in the treatment of gastric ulcer in the 1920's, its routine use in the treatment of duodenal ulcer was initiated in Germany in the early 1920's and not generally accepted in this country until the 1930's. It has stood the tests of evaluation now for more than 25 years and has been used in innumerable thousands of cases. In my opinion, the results following the Billroth II type of partial gastrectomy for chronic recurring duodenal ulcer, gastric ulcer, and gastrojejunal ulcer after gastroenterostomy are superior to those of any other type of surgical procedure for these types of benign peptic ulcerations, as based on the relief of ulcer pain, the functional results, and the infrequency with which recurring ulcer takes place. These results compare very favorably with those of surgical treatment of any other benign intra-abdominal lesion. Should a gastrojejunal ulcer develop after a Billroth II resection, Chance and I [5] found excellent results, with healing of the ulcer occurring in 87% of the cases following transabdominal vagotomy. I agree with a distinguished Scottish surgeon, who, after his gastric resection some three or four years ago, told me he wished he had undergone the operation many years previously, for since the operation he had been able to live a normal life, work as hard as he wished to, eat anything, drink anything, and do anything. If I had a chronic recurring duodenal ulcer with the complications for which the operation is used at the Mayo Clinic, namely, perforation, obstruction, and intractability, I would unhesitatingly accept the advice of my surgeon to have a Billroth II type of gastric resection.

My former first assistant, Dr. Lynn, and I,[6] with the aid of Dr. Berkson, of the Section of Biometry and Medical Statistics, thought it would be a good idea to contrast the results of the Billroth I with those of the Billroth II type of resection in the treatment of gastric, duodenal, and gastrojejunal ulcer when a period of more than five years followed operation. We chose to make the selection from the 5-year period, 1945 to 1950, with a 5-year to 10-year follow-up. The better results to be expected from the Billroth II operation were evidenced by the fact that during this time 729 patients underwent this procedure in contrast to but 185 who underwent the Billroth I procedure.* The recurrence rate among 449 traced patients with duodenal ulcer who underwent the Billroth II resection was

* One reason for more frequent use of the Billroth II operation than of the Billroth I in the treatment of duodenal ulcer was the fact that I found during 1930 and 1940 that the incidence of ulcer recurrence was greater after Billroth I than after the Billroth II.

3.7% (1.6% suspected), while in 27 traced patients who underwent the Billroth I resection the recurrence rate was twice as much, being 7% with a 7% suspected recurrence. For gastric ulcer the numbers in each group undergoing the Billroth I and Billroth II were more nearly comparable, being 139 in the Billroth II and 113 in the Billroth I. The incidence of recurrence was 3% in the former and 4% in the latter, plus an additional 1% who had a suspected recurrence.

In the treatment of gastrojejunal ulcer, however, the greater difference between the two procedures was quite apparent. Gastrojejunal ulcers must be divided into those developing after gastroenterostomy and those after gastric resection.† In the present study, when a Billroth II resection (87 patients) was done, regardless of the location of the recurrence and the type of previous operation, there was an 8% proved recurrence and 3% suspected, whereas when the Billroth I type of anastomosis (26 patients) was made, the recurrence rate was 19% with an additional 8% suspected recurrence. These data are indicative of the reason why many more resections of the Billroth II type were done for duodenal and gastrojejunal ulcers than for gastric ulcer. However, it must be remembered that only about one-fourth the number of patients with duodenal ulcer had had the Billroth I type of resection compared with the Billroth II, and one-third (87 *vs.* 26) those with gastrojejunal ulcer. Hence, for each recurrence in the Billroth I series the comparable percentage is four and three times greater than with each recurrence in the Billroth II series with such lesions.

Functional Results

Lest one forms an erroneous impression as to the advantages of the operation from a discussion of recurrences, let me emphasize the fact that, when the functional results were studied and the excellent and good results were grouped together, the number totaled 92% in the Billroth II type of resection and 88% in the Billroth I type. Moreover, in an elaboration of the functional result, only 2% of the patients, and this was in each series, continued to have severe postgastrectomy symptoms. This was due to the decreased gastric capacity, the lack of the ability to eat large meals, the rapid emptying of the stomach into the small intestine, and the increased rate at which food passes through the small intestine. Although regurgitation of bile into the stomach was slightly commoner in the Billroth II series, we did not feel that our follow-up analysis was critical enough on that point to establish a statistical difference. In essence, then, we were unable to discern a significant difference in the functional results when the Billroth I and the Billroth II series were compared.

Sex Differences

An interesting part of the study had to do with the incidence of the recurrence of the ulcer in the two sexes because of the thought that following the Billroth I type of procedure there might be fewer nutritional disturbances, less dumping, and less loss of weight when a gastroduodenal anastomosis was made than after the gastrojejunal type. We found that there was very little difference in the functional results of the two operations in women as compared with men. Moreover, the incidence of recurring ulcer in women after the Billroth I was proportionately the same as that of men, and the same thing was true in the Billroth II, but here again in considering percentages it must be remembered there were 10 times as many men operated on in the entire series as women, and hence the percentage in women is numerically increased.

Vagotomy With or Without Gastroenterostomy

Satisfactory as the results have been with the Billroth II gastric resection, it is always

† In 1955 Chance, Berkson, and I[5] presented a study of 301 cases of gastrojejunal ulcer, contrasting the results of vagotomy with those of gastric resection.

the duty of the medical scientist to be constantly seeking for improved methods. This was the motivating factor, I am sure, in Dragstedt's[7] studies on the effects of vagotomy in the treatment of peptic ulcer in human beings, and in experimentally produced ulcers in animals, and his later studies on the hormonal secretion from the gastric antrum as a stimulant of gastric-acid secretion. After performing vagotomy in 158 cases between 1943 and 1949 without other procedures on the stomach, Oberhelman and Dragstedt[8] last year reported that there was a 15.8% (25 patients)‡ incidence of recurring duodenal ulcer, gastric ulcer, or ulcerative gastritis, or failure to heal of the duodenal ulcer, and the incidence in gastric ulcer was even higher. When combined with a gastric drainage operation, such as gastroenterostomy, involving 487 patients (1943-1953), the incidence of recurrence and gastric ulceration was 8% (39 patients). The mortality rate was 1.2%. Their follow-up of cases in which operation was performed in 1943 to 1953, it will be noted, was only two years in the shortest follow-up period; and, unfortunately, no data are given of number of patients operated on in the various years.

We began using vagotomy in 1945 after Dragstedt's interesting studies on the results of vagotomy, and later on results of vagotomy and gastroenterostomy, in certain patients with chronic duodenal ulcer on whom surgical procedures were carried out. In 1947,[9] in the 442 patients with duodenal ulcer operated on, 317 (72%) underwent partial gastrectomy. This number increased progressively over the years so that it was 84% in 1955. On the other hand, the percentage of gastroenterostomies has decreased proportionately. In 1947, 55 (12%) underwent gastroenterostomy and 49 (11%) underwent vagotomy and gastroenterostomy. In 1955,[10] but 5% of the patients operated on for duodenal ulcer underwent gastroenterostomy with vagotomy and 4% underwent gastroenterostomy alone.§

The experience of others and of ourselves in cases in which vagotomy and gastroenterostomy had been performed has shown several times the incidence of recurring ulceration that occurs after partial gastrectomy of the Billroth II type. Indeed, it is greater in our experience than after gastroenterostomy when performed alone. At a meeting of the Southern Surgical Association just a few days ago, one of my first assistants, Dr. Mobley,[13] and I presented the results of vagotomy and gastroenterostomy in a group of 209 patients operated on for duodenal ulcer from 1945 through 1949 at the Mayo Clinic. In 79% a 5-year to 10-year follow-up was obtained. Vagotomy alone was performed 31 times; vagotomy and gastroenterostomy, 124 times; vagotomy and pyloroplasty, 7 times, and vagotomy and gastric resection, 4 times. Recurrence proved roentgenologically or at operation took place in 14% of the patients. In the 23 patients of the group with ulcer recurrences, subtotal gastric resection of the Billroth II type was performed in 15, and results have been excellent in 12, satisfactory in 2, and poor in 1. From the standpoint of functional results in the vagotomy group, 72% were asymptomatic or improved (32%, asymptomatic and 40%, improved). Ninety-five patients (including the ulcer-recurrence group), however, had persisting symptoms, such as ulcer-like pain in forty-one (43%), diarrhea in thirty-eight (40%), vomiting in twenty-one (22%), bleeding in twelve (13%), loss of weight in eleven (12%), and dumping in four (4%). The risk of the vagotomy with and without gastric operation was 2%. In

‡ An additional 23 patients (14.5%) were classified by them also as poor results.

§ Five additional patients with duodenal ulcer underwent pyloroplasty.

The lesions were large perforating duodenal ulcers with marked obstruction or sclerotic obstructing duodenal ulcers in older patients with low gastric acids.

The proportion of partial gastrectomies in 1953 was 85.9%, and in 1954 it was 86.7%. In both 1953[11] and 1954[12] the percentage of vagotomy and gastroenterostomy was 6.2%.

the study by Lynn and me of the Billroth I it was 1.2% (5-year to 15-year series)[14] and 1.7% in the Billroth II (5-year to 10-year series). It can be seen from this statistical study that the risk of operation in the cases chosen to have this procedure rather than partial gastrectomy was practically the same as for partial gastrectomy. Hence, with the high incidence of recurring ulceration and with postoperative persisting complications of the type mentioned, including 11% of the patients having loss of weight and 4% having dumping symptoms, one is justified in concluding that vagotomy with or without gastroenterostomy in the treatment of duodenal ulcer has several disadvantages when compared with results that follow partial gastrectomy.

Gastroenterostomy

What about gastroenterostomy itself, without the addition of vagotomy? A recent report by Farquharson,[15] surgeon in the Royal Infirmary at Edinburgh, in seeking for better results in the treatment of duodenal ulcer, cited the statistical studies published between 1929 and 1935 by Luff, Balfour, Benedict, Walton, and Wright, in which the total number of cases reported on was 5170, with an average proportion of stomal ulcer of 3.5%. In discussing these data, Farquharson said, "If we believe as many do that the incidence of stomal ulcer after gastrojejunostomy is much higher than that recorded in these series, either we must hold that the period of follow-up was inadequate or we must admit that we cannot get such results nowadays." I think that the explanation of variations in percentages in these cases as compared with what are being reported at the present time, in what was reported by some of the approximately 12% to 14% recurrence, is probably based on a much longer follow-up study than was used in the collected series of cases by the authors I have referred to. Be that as it may, Farquharson pointed out the following in his arguments for a reevaluation of the operation of gastroenterostomy at the present time: "Let us accept—but only for the purpose of argument—that the incidence of stomal ulcer is 10 per cent, 15 per cent, or even 20 per cent and then let us assess the position of a patient who has acquired such an ulcer. Twenty years ago this was a very serious complication, for Wright (1935) recorded a mortality rate of 28 per cent from various operations used in treatment, together with a further 12 per cent of deaths due to the ulcer itself. Now the position has entirely altered, for treatment has become standardized in the operation of partial gastrectomy." Farquharson continued, "Tanner (1954) had only 1 death in 107 cases—a mortality rate actually lower than that which he records for partial gastrectomy in uncomplicated cases of gastric and duodenal ulcer." In a larger series of cases Tanner's mortality rate would most certainly have equaled his mortality rates for an equal number of similar operations for uncomplicated gastric and duodenal ulcers, and this has been the experience of my colleagues and myself.

In 1955 at the Mayo Clinic (Waugh, Walters, Gray, Priestley, and Judd)[10] partial gastrectomies were done for gastrojejunal ulcer in 36 cases‖ with a mortality rate of 2.7%.¶ It is this operation which we prefer to vagotomy in cases in which recurrences developed after gastroenterostomy, because the results, as Chance and I reported, are considerably better than for vagotomy (86.5% had excellent results). However, in some cases where the area of anastomotic ulceration is small and its healing following vagotomy would not obstruct the gastrojejunal anastomosis, and/or where the condition of

‖ Four patients underwent associated vagotomy. Ten vagotomies were done without gastric resections with no deaths.

¶ In Chance's and my report in 1955 of patients operated on between 1945 and 1952, in the 186 patients with gastrojejunal ulcer after gastroenterostomy there was a 0.5% mortality rate. One hundred forty-five underwent gastric resections with one death, a mortality rate of 0.7%. Twenty-nine had vagotomy alone; three had vagotomy plus gastric resection, and nine had vagotomy and other operations.

the patient would not seem to warrant the greater risk of partial gastrectomy, vagotomy alone has given excellent results in 77.8% of the cases, a very creditable showing. However, when the recurrence developed after partial gastrectomy, the results of vagotomy were superior to re-resection, and the operative risk was less. I would like to note particularly this sentence quoted from Farquharson's article, "Indeed, as Wells (1955) points out, it was the excellent results of partial gastrectomy for stomal ulcer that converted British surgeons to this operation as the primary treatment of duodenal ulcer." The good result from partial gastrectomy in Britain and other countries has also been the experience of my colleagues and myself at the Mayo Clinic, and, I believe, of most American surgeons, and we see no reason to change our method of surgical procedure at the present time. We do acknowledge that gastroenterostomy in certain patients with large, chronic, penetrating duodenal ulcers is an operation which may be preferable to partial gastrectomy. This preferability results from the lowered risk by not attempting to remove the area of duodenal ulceration because of the risk of leakage from the duodenal stump with serious complications resulting, and it may be the indicated procedure in the elderly patient with large ulcers and low acids or in cases of a burned-out duodenal ulcer in which the healing scar has obstructed the duodenum.

Colonic and Jejunal Replacement

I would not be completing my discussion of peptic ulcer unless I referred to two contributions of the last few years. The first has to do with colonic or jejunal replacement of the resected stomach, as advocated by Moroney[16] and Henley.[17] Moroney transposed a segment of transverse colon between the resected stomach and the duodenum, and Henley a segment of jejunum, the idea being to afford greater capacity for the retention of food and a slower emptying into the duodenum. At first these procedures gave very encouraging results; the patients gained in weight, and there seemed to be fewer dumping symptoms. The early reports of these investigators seemed to indicate that there was real value to the procedure, but with the passage of a year or two more both reported an incidence of recurring ulceration of approximately 8%, which might have been anticipated, since the interposed segment did nothing to further reduce gastric acidity, nor did it change the physiologic aspects of gastric secretion and neutralization.

Finally, I should like to say a word about the tubular gastric resection of Wangensteen. In 1929 Connell[18] suggested gastric fundusectomy as a physiologic method of reducing gastric acidity. He excised a pie-shaped segment from the corpus and fundus, removing approximately 40% of the stomach. Between 1938 and 1940 Wangensteen[19] removed a somewhat larger area by excising more of the greater curvature. He postulated, as had Connell, that tubular gastric resection removes a larger portion of the acid-secreting mucosa of the stomach and hence that the duodenal ulcer should heal. Experimentally, he protected dogs against histamine-induced ulcer with this type of operation. In his preliminary evaluation of the method in January, 1953, in tubular resections on 51 patients, he wrote[20] that free hydrochloric acid was present in 50% of the cases after the operation, that hypochromic anemia had not occurred, but that 80% of the patients had lost weight, that diarrhea was less frequent than after the usual gastric resection, and that recurring ulceration had possibly occurred in one patient. In a personal communication to me[21] in January, 1955, Wangensteen stated that he and his colleagues had done 150 tubular resections and 100 segmented resections # and that there had not been a single bona fide recurring ulcer. However, he did not mention physiologic studies of preoperative and postopera-

Associated simultaneous pyloroplasties of the Heineke-Mikulicz type were also performed in these cases.

tive gastric acidity or fluoroscopic or roentgenographic studies of motility.

It is the opinion of my colleagues and me that this surgical procedure is still in the investigative stage and that insufficient time has elapsed since the operation and an insufficient number of cases have been observed to insure an accurate estimation of recurrent ulceration and the functional results of the operation. I would suspect that, with an incidence of achlorhydria of only 50%, the incidence of recurring ulceration with the passage of time will be found to increase proportionately to a Billroth I resection where a similar amount of stomach has been removed, for I have found that approximately 50% of such patients also have free hydrochloric acid and the incidence of recurrence is several times higher than for the Billroth II resection, where 72% to 75% develop a postoperative achlorhydria.

Comment

It is obvious that in our evaluation of peptic ulcer therapy from the surgical standpoint, based on a follow-up of patients operated on between 1945 and 1950, the Billroth II type of gastric resection * for chronic recurring duodenal ulcer has given the best results for men and women, as measured by relief of symptoms, the functional results which have followed, and the low incidence of recurrence of ulcer. When a similar amount of stomach was removed and a Billroth I was performed, the functional results were not of greater superiority over the Billroth II to overcome the disadvantages of a two and three times incidence of recurring ulceration, and this was true regardless of the sex of the patient.

In the treatment of gastrojejunal ulcer developing after gastroenterostomy, although the Billroth II type of gastric resection with removal of the gastrojejunal ulcer and the gastroenteric stoma gave results superior to those that followed the Billroth I type, vagotomy in certain but fewer cases did give excellent results. In chronic recurring gastric ulceration, the results of both the Billroth I and the Billroth II resections were about the same.

There is a place for gastroenterostomy in certain types of large, penetrating, obstructing duodenal ulcers, particularly in patients with low or average gastric acids or in elderly patients with burned-out sclerotic ulcers and low acids. However, the long-term results of such a procedure, even when vagotomy has been added, have not compared favorably with those of partial gastrectomy. In such cases, that is, gastroenterostomy and vagotomy, the incidence of recurrent ulcer was four times that occurring after partial gastrectomy. Moreover, the functional results which followed the procedure of gastroenterostomy and vagotomy presented many unpleasant postoperative sequelae, which were not present to any such extent following gastric resection, and the incidence of dumping disturbances or of disturbances of the nutritional state was about the same in the two groups, regardless of sex.

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* Two-thirds to three-fourths resection.

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Intestinal Obstruction Simulated by Nonobstructing Intra-Abdominal Lesions

Report of Two Cases

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The diagnosis of large or small bowel obstruction has been discussed in modern surgical texts, and the method of therapy has been adequately outlined. There are, however, occasional patients in whom a preoperative diagnosis of intestinal obstruction is made but in whom, at the time of laparotomy, a lesion situated outside the gastrointestinal tract is found responsible for the symptom complex and physical findings of intestinal obstruction. In these cases mechanical obstruction is not present.

Two cases have been encountered recently at The New York Hospital illustrating a symptom complex compatible with intestinal obstruction without actual mechanical obstruction being present. A brief review of the literature and discussion is presented. These cases exhibited acute intra-abdominal pathology, which was situated close to the gastrointestinal tract so that an inflammatory process caused reflex segmental ileus and a clinical picture of mechanical intestinal obstruction.

Report of Cases

CASE 1.—A 77-year-old white man entered The New York Hospital on Jan. 20, 1954, with a chief complaint of having had abdominal tenderness and distention of the abdomen for three days. One year prior to admission a right inguinal hernioplasty was performed at The New York Hospital. His past health had been excellent. Three days before admission, upon retiring, he noted a generalized abdominal tenderness which was made slightly worse with motion. His abdomen became distended the following morning and anorexia became marked, although he did not vomit. Two days prior to admission, two enemas produced a small amount of feces and considerable gas; however, the abdominal distention and tenderness continued. Occasional small amounts of gas were passed spontaneously per rectum but ceased 24 hours before admission. There were no recent changes in bowel habits; there had been no weight loss. The patient had experienced "marble-like" stools for years, and there was no recent melena, diarrhea, or constipation. There was no history of food intolerance, chills, fever, or jaundice in the past.

Physical examination revealed a temperature of 37 C (98.6 F); pulse rate, 92; respirations, 16; blood pressure, 120/70. The patient was a well-developed thin, white, slightly dehydrated man in moderate distress. Positive physical findings were mild pulmonary emphysema, bilateral lenticular opacities, and an enlarged prostate. The abdomen was markedly tender, without localization. Tympany was generalized. There were no masses or organs palpable. Hyperactive bowel sounds with occasional peristaltic rushes were heard throughout the abdomen. There was neither a fluid wave nor shifting dullness. Laboratory data: The urine was amber and clear, with specific gravity of 1.018. There was 2+ albuminuria. Microscopic examination of centrifuged sediment was negative. Complete blood count revealed the hemoglobin to be 16.5 gm.; red blood cell count, 5,600,000; white blood cell count, 16,100, with a differential count of 21% lymphocytes, 4% monocytes, 68% mature polymorphonuclear leukocytes and 7% band polymorphonuclear leukocytes.

Roentgenographic examination shortly after entry consisted of plain films of the abdomen, both supine and erect. The report was "enormously dilated small bowel loops arranged in a stepladder fashion across the center of the abdomen. There is also noted gaseous distention of the large bowel, the ascending and

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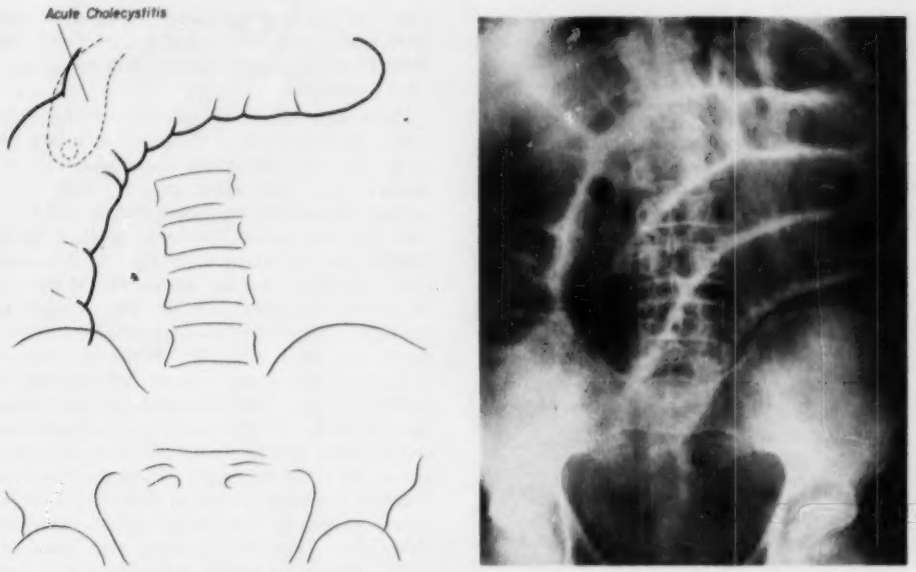

Fig. 1 (Case 1).—Upright roentgenogram and tracing demonstrate stepladder dilation of small bowel and dilated ascending and transverse colon. These are no fluid levels or free air. The radiopaque gall stone is visible in the right upper quadrant.

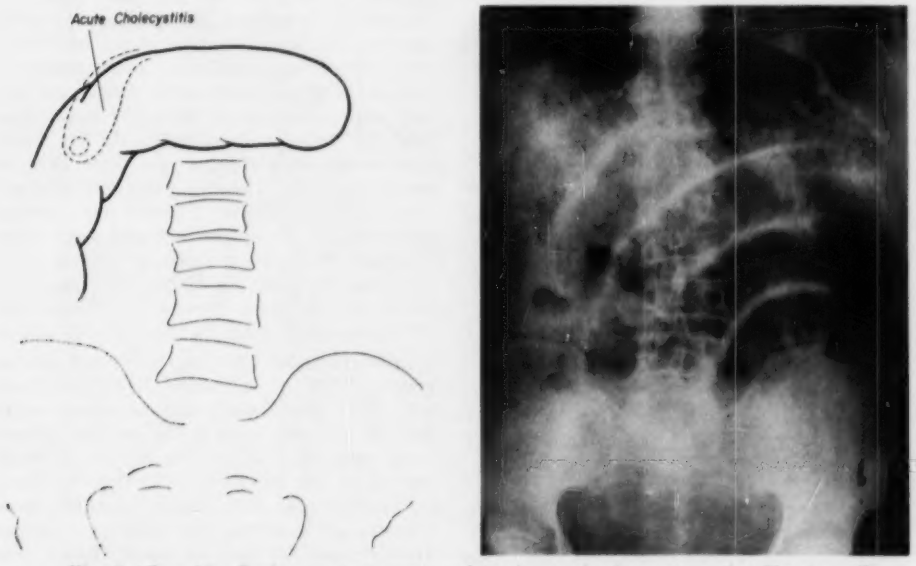

Fig. 2 (Case 1).—Supine roentgenogram and tracing again demonstrate the dilated small bowel and the dilated ascending and transverse colon. The approximate position of the gallbladder is shown.

transverse portions only being visualized distended with gas. Beyond the splenic flexure no visualization of gas-filled large bowel is demonstrated. There is no evidence of fluid in the upright position of either of the films. There is also noted a 1 cm. calcific density overlying the right 11th rib posteriorly which may represent a stone in the gall bladder or may represent opaque medication. Impression: Probable mechanical obstruction with site at

splenic flexure. There is large and small bowel gaseous distention without evidence of fluid level."

Course: The patient received intravenous fluids to correct his dehydration. The findings were compatible with intestinal obstruction due to carcinoma of the splenic flexure, and on the night of admission the patient was subjected to exploratory laparotomy (Jan. 20, 1954).

Summary of Operation.—The peritoneal cavity was entered through an upper right rectus muscle-splitting incision. The transverse colon was moderately distended, but palpation of the left side of the abdomen failed to reveal an obstructing lesion. In the upper right abdomen there was an acutely inflamed distended gallbladder. There were adhesions to the duodenum and omentum, but these did not cause obstruction of any hollow viscus. The gallbladder was removed. The common duct was not enlarged.

The surgical pathological report was cholecystitis, chronic, with acute exacerbation and cholelithiasis.

The patient's recovery was uneventful, and he was well on examination two years after the operation.

Comment.—This man was essentially well until the onset of acute generalized abdominal pain and distention. There were no symptoms of gallbladder disease. Abdominal pain and distention, anorexia, nausea and vomiting, and obstipation combined with the physical findings of abdominal distention and hyperactive peristalsis were compatible with the diagnosis of intestinal obstruction. The roentgenograms seemed to confirm the clinical impression.

The only pathological process noted at exploration was an acutely inflamed gallbladder containing calculi. The gallbladder did not mechanically obstruct the lumen of the colon.

CASE 2.—A 73-year-old white man was admitted Sept. 18, 1954, and complained of having had vomiting, abdominal distention, and abdominal pain for three days. In 1943 subtotal thyroidectomy had been performed for "colloid goiter." He had been hospitalized for treatment of bronchopneumonia in 1946, with an uneventful recovery. In February, 1954, seven months prior to his present illness, he had suffered a cerebrovascular accident and was noted to have arteriosclerosis and arteriosclerotic heart disease. He had recovered well and received supportive and modified custodial care from The New York Hospital outpatient and social service departments.

Three days before the present admission, he noted sudden onset of bloodless vomiting for 24 hours. Two days before admission he developed steady left upper quadrant pain which radiated posteriorly into the left flank and back. The pain was colicky and was relieved by an injection by his family physician. At this same time, 48 hours before admission, abdominal distention was noted and was most evident in the upper abdomen. Two soapsuds enemas produced no feces or gas. He was anorexic throughout this acute episode and vomited all ingested fluids. The distention and abdominal pain increased on the day prior to admission, and he came to The New York Hospital emergency room for treatment. There had been no previous anorexia, nausea or vomiting, food intolerance, weight loss, symptoms of jaundice, or melena. There was nocturia two times per night. He had no cardiac symptoms other than dyspnea on climbing two flights of stairs.

Physical examination revealed a temperature of 37.6 C (99.7 F) (p. r.); pulse rate, 100 (regular); respirations, 20, and blood pressure, 180/140. He was a well-developed well-nourished elderly man suffering acute abdominal distress. He was moderately dehydrated and had numerous rales in the right lower lung field. The heart was enlarged to the left. There was normal sinus rhythm, and there were no murmurs. The abdomen was protuberant, tense, and tympanitic. There was marked tenderness in the epigastrium and both upper quadrants, more being noted in the left upper quadrant. Rebound tenderness was equivocal. Bowel sounds were present but hypoactive. There was slight pitting edema of both ankles.

Laboratory data: Urinalysis showed specific gravity, 1.020; 3+ albuminuria; 0-2 red blood cells; 10-15 white blood cells, and several coarse and fine granular casts in the sediment. Blood count revealed 17.9 gm. hemoglobin, 6,000,000 red blood cell count, and 22,500 white blood cell count, with 80% mature and 6% band forms of polymorphonuclear leukocytes. Venous pressure was 220 mm. of water. Blood urea nitrogen was 16 mg/100 cc.; sodium, 108 mEq/liter; potassium, 5.0 mEq/liter; bilirubin, 1 mg/100 cc. EKG was reported to be essentially normal.

Roentgenogram of the chest revealed heavy bronchovascular markings which possibly represented pulmonary congestion, and there was associated generalized cardiac enlargement.

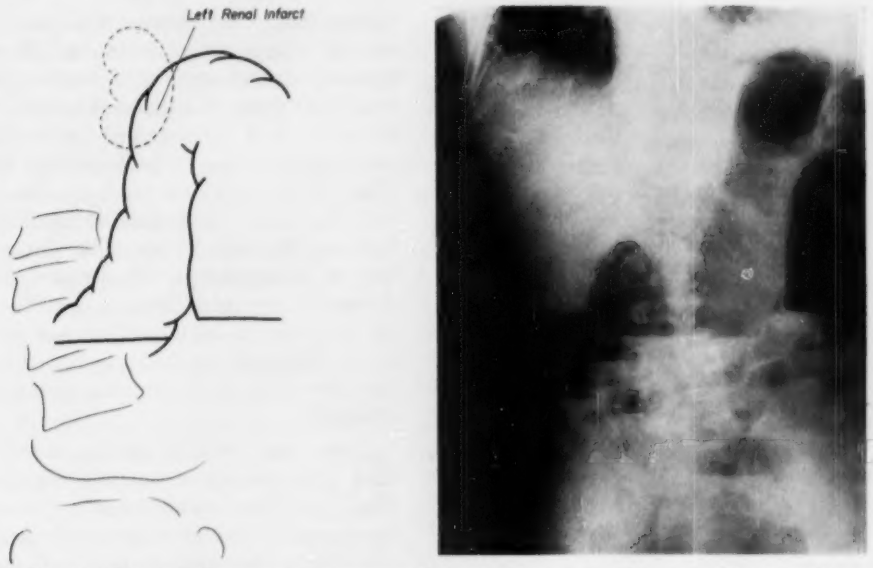

Fig. 3 (Case 2).—Erect roentgenogram and tracing demonstrate loops of dilated small bowel and dilated transverse colon and descending colon. Fluid levels are evident. The tracing indicates the approximate position of the infarcted kidney.

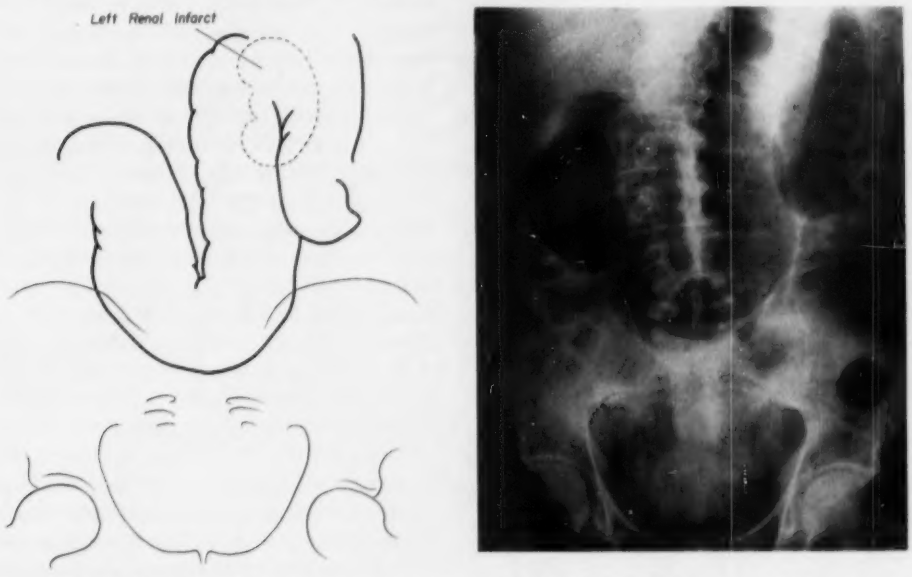

Fig. 4 (Case 2).—Supine roentgenogram and tracing outline the dilated colon and its relation to the infarcted kidney.

Plain and upright abdominal films demonstrated gaseous distention of the large bowel, with many fluid levels in the upright film. There was no gas in the rectum, and the radiologist reported that the findings were strongly suggestive of mechanical obstruction in the lower descending or sigmoid colon.

Course: Because there was evidence of early congestive heart failure, the patient was rapidly digitalized with lanatoside C (Cedilanid). In-

travenous fluids were administered cautiously to correct his dehydration and hyponatremia. Laparotomy was performed on the day of admission, because mechanical obstruction of the distal colon was believed to be present.

Summary of Operation.—The abdomen was entered through a right upper rectus muscle-splitting incision. The transverse and right colon were markedly distended. The small bowel was not distended and was unremarkable when examined in its entirety. Careful examination of the left colon failed to reveal the suspected obstructing lesion. The right upper pole of the kidney contained a 2 cm. firm mass, but this in no way impinged on the lumen of the bowel. The remainder of the exploration was negative, and a transverse colostomy was performed.

Course: The colostomy was opened on the second postoperative day and functioned well. The abdominal distention decreased progressively, and oral intake was resumed. Urinary output was adequate. Eight days after surgery, the patient suddenly developed a left hemiparesis, but he was well oriented. Fifteen days after surgery, one week after suffering the cerebral thrombosis, he suddenly lapsed into coma and remained comatose and unresponsive. He died three weeks later, five weeks after abdominal exploration.

Autopsy.—There was generalized arteriosclerosis, with thrombosis of the left internal carotid and right middle cerebral arteries. There were multiple old and recent cerebral infarcts. There was a complete thrombosis of the left renal artery, with old and recent infarction of the left kidney. The left kidney was purple and mottled, and there was marked necrosis of the parenchyma of the kidney. There were bilateral adrenal infarctions and generalized bronchopneumonia. The small and the large bowel were unremarkable except for the presence of the surgically established transverse colostomy.

Comment.—This elderly man with a history of recent cerebral thrombosis developed symptoms and signs of acute intestinal obstruction. Roentgenograms illustrated a sharp "cut-off" point in the descending colon. The only pathological finding at autopsy was a left renal infarction due to a thrombosis of the left renal artery. The bowel was normal.

General Comment

In infants and children various syndromes of intestinal obstruction have been displayed without mechanical obstruction being discovered at laparotomy. Zuelzer and Wilson [1] reported 11 such cases of functional intestinal obstruction characterized by vomiting, distention, and constipation. In many of these, aganglionosis of the bowel was found when the specimen was studied microscopically. Rack and Crouch [2] and Forshall, Richham, and Mossman [3] reported this functional type of obstruction in the newborn. They discounted meconium ileus as the cause of the syndrome, as all the infants had normal bowel movements in the early postnatal period prior to onset of symptoms of intestinal obstruction.

There have been several reports [4,5,7] of acute inflammatory intra-abdominal conditions producing "sentinel loops" of bowel in the region of the inflammatory lesion, and occasionally these patients have presented a classical picture of intestinal obstruction prior to surgery or inception of nonoperative therapy.[6-8] Paxton and Payne noted that 26 patients in a series of 307 cases of acute pancreatitis had an admission diagnosis of "intestinal obstruction," though this was not further described or illustrated in their report. It is thought that the localized peritonitis surrounding the inflamed pancreas produced a segmental ileus and led to the diagnosis of intestinal obstruction. Ferguson [9] reported two cases of acute cholecystitis associated with "stasis of the large bowel." Both had distended large intestine—from the cecum to the hepatic flexure—and in the second case bowel sounds were noted on physical examination, a finding which further substantiated the diagnosis of intestinal obstruction. The syndrome of "spastic ileus" has been described.[10-12] This condition consists of persistent contraction of one segment of large bowel musculature with obstruction of the bowel proximal to this segment. The etiology has been identified variably as trauma, hysteria, systemic infection, lead poisoning, or neoplastic invasion of the coeliac plexus by neoplasm (Ogilvie's syndrome of false colonic obstruction).[12] In many cases no pathological proc-

ess was found, and it was believed that anesthesia had relieved the muscle spasm. In others the spastic segment was resected, with normal microscopic findings on pathological examination.

Mayo [13] reported a 48-year-old man with abdominal pain and distention who had a dilated large bowel with no gas in the sigmoid colon or rectum. The patient died suddenly, and dissecting aneurysm of the aorta with rupture and intraperitoneal hemorrhage was found at autopsy.

Shelly [14] reported marked dilatation of the colon following development of an abdominal aortic aneurysm. Barium enema revealed a normal colon, and anal dilatation relieved the colonic distention. Prior to barium examination intestinal obstruction was suspected. Superior mesenteric artery thrombosis has produced a picture of large bowel obstruction,[15] with the dilatation of the colon ending abruptly at the distal transverse colon.

Hinton,[16] in discussing the surgical significance of acute abdominal pain, notes that retroperitoneal hemorrhage from trauma may frequently mimic organic bowel obstruction. In many of these previously noted reports, it seems obvious that a segmental type of ileus with inability of the bowel to propel the intestinal gas and fluid has led to the diagnosis of mechanical obstruction.

In 1929 Alvarez and Hosoi [17] postulated the cause for failure of the unobstructed bowel to transport its contents, and their conclusions were based upon loss of one or more of the three types of normal peristaltic activity caused by influence of extraintestinal elements. The loss of normal gradient of intestinal activity in passage into the distal bowel well explains how many of these aforementioned lesions led to a diagnosis of intestinal obstruction.

Two cases of extragastrointestinal disease mimicking intestinal obstruction have been presented. In one, acute cholecystitis and, in the second, left renal infarction produced the syndrome of intestinal obstruction. In both instances the site of obstruction was thought to be in the colon. It should be noted that the presumed site of obstruction was not in close spatial relationship to the neighboring inflammatory process. In both instances the dilated colon extended a relatively long distance from the site of inflammation. In the case of acute cholecystitis, the distended colon extended to the splenic flexure, and in the case of left renal infarction dilated colon extended to the mid-descending colon. Both were apparently due to reflex ileus and were caused by the process in close proximity to the bowel. It is interesting that the syndrome of acute intestinal obstruction was so well simulated by these lesions. In retrospect it is difficult to suggest that any other diagnosis could be made in these cases prior to operation. The clinical picture in each instance was supported by laboratory data. Bowel sounds were present in both, and in one they were found to be hyperactive.

One must conclude that in certain instances reflex ileus can simulate organic intestinal obstruction. Localized intraperitoneal or retroperitoneal inflammatory processes may cause localized segmental paralytic ileus, thus producing syndromes such as these.

When an obstructing lesion is not found at the time of exploratory laparotomy for suspected intestinal obstruction, the retroperitoneal areas and all neighboring intraperitoneal viscera should be carefully inspected.

Summary

Two cases of acute inflammatory lesions are presented. These lesions produced a clinical and laboratory picture of mechanical large bowel obstruction.

They are reported to emphasize the need for careful preoperative diagnostic work-up and careful exploration of the bowel and its surrounding organs at operation should an obvious mechanical obstruction not be present at the time of exploration.

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Books

Although the A. M. A. ARCHIVES OF SURGERY *does not customarily publish book reviews, the value of such reviews is recognized, and from time to time the Editors will publish reviews of outstanding works in the field of medicine and surgery and other medical sciences. At the request of the Chairman of the Editorial Board, the two-volume work of the American Foundation, "Medical Research: A Midcentury Survey," has been reviewed by a distinguished American surgeon, Prof. I. S. Ravdin, of the University of Pennsylvania. It gives the Editors of the* A. M. A. ARCHIVES OF SURGERY *pleasure to publish Dr. Ravdin's review on this important study.*

WALTMAN WALTERS, M.D.
Chairman, Editorial Board
A. M. A. ARCHIVES OF SURGERY

Medical Research: A Midcentury Survey (Vol. 1, American Medical Research in Principle and Practice; Vol. 2, Unsolved Clinical Problems in Biological Perspective). By the American Foundation; Member-in-Charge, Esther Everett Lape; Committee of Consultants: Walter Bauer, George H. Bishop, Austin M. Brues, George W. Corner, René J. Dubos, C. A. Elvehjem, Louis F. Fieser, Thomas Francis Jr., Ralph W. Gerard, Michael Heidelberger, William G. Lennox, Esmond R. Long, William S. McCann, Thomas Parran, Linus C. Pauling, John P. Peters, I. S. Ravdin, Francis O. Schmitt, Truman G. Schnabel, W. M. Stanley, DeWitt Stetten Jr., E. L. Tatum, Stafford L. Warren, Paul A. Weiss, M. C. Winternitz, and John B. Youmans. Price, $15 for two-volume set. Little, Brown & Company, 34 Beacon St., Boston 6, 1955.

The Surgeon's Stake in Basic Research

The American Foundation's "Medical Research: A Midcentury Survey" develops, throughout what the London *Lancet* describes as "two fascinating volumes," the thesis that progress in clinical medicine depends upon continual basic research in laboratories of biology, chemistry, physics, and atomic energy. This message is addressed as directly to the surgeon as to the internist. The survey reflects a realization (which some of us have long been stressing) that the amazing development of modern surgery is due less to increasingly ingenious techniques and increased dexterity on the part of the surgeon than to surgery's increased concern with normal physiologic and metabolic mechanisms and derangement of these mechanisms under the assault of disease and of operative trauma.

Not that the ingenious techniques are to be lightly rated; in cardiac and pulmonary surgery, for instance, ingenuity has gone very far in clearing the operative field by devising mechanical means for doing the work of the heart and for oxygenating blood as the lungs do. But successful use of these devices has also shown that much more than mechanics must be considered in finding a satisfactory substitute for the heart-lung system as an essential part in the living organism.

Thus, surgical science depends less upon ability to perform technical feats and more upon ability to maintain the patient in balance, that is, upon the surgeon's knowledge of nutrition and metabolism, of protein requirements, of fluid and electrolyte regulation, of endocrine balance and replacement expedients, of biochemistry of nerve and muscle activity. This is knowledge that results only from continual basic research and the surgeon's access to it.

No surgeon concerned with the essential relation between surgery and physiology could fail to salute, as an index of progress, the American Foundation's astoundingly comprehensive and sound review of present trends in basic research pertinent to medicine. Current increased demands for more basic research and current increase in public and private funds for medical research stressing basic research lend especial timeliness to the Foundation's report. From various parts of the country, in government research institutes, in universities and medical schools, policy-making committees report use of this survey in their efforts to define the over-all needs of research, to assess the comparative claims of completing research areas, and to chart the financing of research according to this evidence. Study of the volumes is

reported in group meetings and seminars through which curricular committees are forecasting pertinent lines of research. Health departments in foreign countries, reaching to India and Thailand, have commented upon the aid they find in this discussion of principles underlying the organization and financing of research. While it is the American picture that is presented in the discussion of research principles and practices in the first volume, the discussion is applicable to research anywhere. It is important to have funds for research. It is even more important that the funds should be applied to those broad main currents of basic research most likely to point to solution not of one or a few but of many medical problems. What areas of research would surgeons now suggest if they were asked to name the fields of research most fundamental to the progress of surgery? These areas would be, I think, the broad lines of fundamental research illustrated in the second volume of this report as most likely to throw light on all the outstanding unsolved clinical problems.

"Almost every facet of the complex that makes for medical advance," according to the editor of the *Lancet*, "is examined in a study which has been in process for fifteen years and which may have as much influence on American medical research as Flexner's reports of forty years ago had on American medical education."

The Committee of Consultants (of which I am a member), which joins the American Foundation's member-in-charge, Esther Everett Lape, in presenting the books, is composed of outstanding basic science investigators and leading medical men, including two Nobel laureates in chemistry, the chairman of the National Research Council's division of biology, two former chairmen of the Council's division of medical sciences, a vice-president of the National Academy of Sciences, the director of the division of biological and medical research of the Argonne National Laboratory, two members of the Rockefeller Institute for Medical Research, the director of a department of the Carnegie Institution of Washington, a former Surgeon General of the United States Public Health Service, an associate director in charge of research of one of the Federal government's Institutes of Health, and ten professors in as many universities (biology, organic chemistry, immunochemistry, biochemistry, neurophysiology, surgical research, medicine), of whom two are deans and one is a former chairman of the certifying board for internal medicine. This committee, while disclaiming credit for actual authorship, which belongs entirely to the Foundation, enthusiastically endorses the *Science* editor's recent description of the book as "an impressive stock-taking and direction-pointing analysis." It endorses Chester Keefer's reference to the report as a "superb summary—the most important and outstanding contribution to the study of medical research in our time. No one, whether he be a doctor, a research worker, a philanthropist, a statesman or a scientist, can afford to be without this work."

In its preparation the Foundation acknowledges a significant debt not only to the critical service of its Committee of Consultants but also to hundreds of individual investigators, to directors of research in universities, medical schools, research institutes, industrial organizations, scientific societies, national voluntary health associations, governmental departments and divisions including the Federal research institutes, the National Academy of Sciences, the National Research Council, the Atomic Energy Commission, the National Science Foundation—most of whom furnished reports especially prepared for this survey. On the basis of these reports and the Foundation's long study over 15 years, the first volume of the report discusses the characteristic contribution of each of these agencies, the methods of organization and financing of research in each. Stressing its usefulness to the surgeon or internist trying to "keep up" with scientific developments, the *Journal of Bone and Joint Surgery* says of this survey, "The information given here could save a would-be researcher reams of correspondence and miles of travel."

While the report, as implied earlier, does not at any point set out to discuss surgical problems separately or, indeed, to imply distinction between the surgeon's problems and those of his nonsurgical colleagues, it is possible to single out from the report certain research problems that are of especial concern to surgeons. These include, for instance, research problems posed to surgeons among others by the miraculous antibiotics. They are cited as illustrating not only a research triumph but also the need of further basic research and, indeed, the danger of any application that is not oriented by continuing research. While accomplishing their miracles in suppressing specific infectious organisms, the Foundation study observes, the antibiotics have also raised fundamental biological questions. The present practice of using them in all infections, minor as well as major, and of using them seriatim in the hope that, if one of them does not reach a particular organism another will, is not, as basic workers and

practitioners alike know, based upon a demonstrated relation between the condition treated and the efficacy of the particular antibiotic.

Perhaps the greatest present challenge of the antibiotics to basic research noted in the Foundation's report is ultimate emergence of resistant strains of organisms in infections that had at first responded to one or several combinations of antibiotics. The report mentions a hospital in which five months after the introduction of erythromycin the proportion of erythromycin-resistant staphylococci in the personnel rose from 0% to 75%. "As each antibiotic is introduced," Dowling observed recently, "we hear first of miraculous cures, secondly of deleterious reactions and then of the appearance of resistant strains." Esmond Long sometime ago pointed out that streptomycin research in tuberculosis "has raised more problems than it has answered." The answer lies not in discontinuing empirical use of the antibiotics but rather in intensive contemporaneous pursuit of the fundamental laboratory research which will finally elucidate the antibiotic mechanism and the reasons for resistance to the drug. At one conference in a recent year 10 new antibiotics and many new combinations were reported. This situation emphasizes the need of regarding each successive antibiotic "discovery" only as one further evolutionary step toward more fundamental knowledge.

The Foundation's Survey of Basic Research Pertinent to Specific Clinical Conditions

The second volume of "Medical Research" illustrates the truth that basic research offers the best—and perhaps the swiftest—hope of solving all clinical problems. This volume reviews lines of fundamental research that have bearing on nine clinical conditions (the nine are selected only for purposes of illustration): cancer; infertility; arteriosclerosis; hypertension; rheumatic syndromes; tuberculosis; viruses and virus diseases; alcoholism, and schizophrenia.

Space available to me here does not permit even a brief review of the basic research touched upon in each of these chapters, all of which are of immediate interest to the surgeon. This may be especially true of the chapter on cancer, a field in which surgery plays so large a part, for experience has inevitably led the surgeon to realization that the fundamental problem is not merely to experiment with therapeutic possibilities but to penetrate to the metabolic fault that changes the mechanism of normal, controlled cell division and growth into mechanisms of uncontrolled growth and malignancy. The cancer chapter, as Austin Brues puts it, "brings into full perspective the increasing impact of basic science on medicine," involving many research areas including studies of chemical carcinogens, of the role of hormones, of the nature and function of nucleoproteins, of nucleic acid, of enzymes, and of viruses. While extirpation of cancerous tissue alone or in conjunction with radiotherapy is at present the best available regimen, and while the possibilities of this regimen have been by no means exhausted, the surgeon nevertheless recognizes its limitations and the consequent need of aligning himself with other investigators in study of the characteristics of cancerous tissue and its failure to conform with normal cellular organization and with mechanisms involved in energy-producing metabolism. If removal of the pituitary will in a fair proportion of cases arrest cancerous growth and/or metastases, few would deplore empirical trial of it, but the central problem remains—to understand the mechanisms responsible for this result and why the procedure sometimes succeeds and sometimes fails.

Surgeons concerned with obstetrics and gynecology will have especial interest in the review of basic research bearing on the clinical problem of infertility. The chapter defines infertility (a nondescript term usually applied to the result rather than to the wide range of serious causes) as including not only sterility but also loss of the products of conception through spontaneous abortion, prematurity, congenital defect. It is to be remembered that maternal, infant, and fetal death add up to the third leading cause of all deaths in this country. The basic work related to understanding fertility and infertility is concerned with the quality of germ plasm in both sexes, the biochemistry of the male and female tracts, the chemistry of fertilization, the physiology of pregnancy, especially of the placenta, and the role of neural, endocrine, and vascular factors in initiating labor. As in all the other chapters of the second volume, centers in which work along these lines is at present being done are concretely noted. The "accuracy and balance" of the discussion of basic work in infertility have been commented upon by George W. Corner, chairman of the National Research Council's committee for research on problems of sex. J. P. Greenhill (senior attending obstetrician and gynecologist, Michael Reese Hospital; editor, "Year Book of Obstetrics and Gynecology"), after describing the whole survey as "prodigious and stimulating," says of the infertility chapter in particular,

"After reading this fascinating chapter, it is disheartening to see how many millions of dollars are devoted to such well-publicized illnesses as cancer and poliomyelitis and how little is spent on the study of sterility, prematurity, anoxia, congenital defects, and fetal and neonatal deaths." It is clear that the causes of failure in human reproduction—failure in conception, spontaneous abortion, premature birth, stillbirth, neonatal death, congenital abnormality—lie close to the common center of all life, cellular biology. Illustrating the truth that the main currents of basic research related to one clinical problem are sure to throw light also on others is the fact that basic research findings pertinent to study of human infertility lie in the same areas of biology, biochemistry, endocrinology, neurology, and genetics from which are drawn basic concepts pertinent to cancer, viruses and microbiology in general, and cardiovascular diseases.

Since, as earlier indicated, "Medical Research" is concerned not with therapeutic approaches but rather with the fundamental investigative work that will furnish the surgeon with needed knowledge of normal and abnormal physiology and thus guide his therapeutic efforts, direct references to surgical procedures are few. When they do occur, as in the references to sympathectomy in the chapter on hypertension, they are mentioned chiefly because of their possible bearing on fundamental mechanisms.

Of unusual interest in the final chapter in the second volume on the biology of schizophrenia (selected merely as the number one problem in the mental field) is brief discussion of the hypotheses that underlie the various forms of lobotomy, lobectomy, topectomy, etc., included in the anomalous term "psychosurgery." This discussion naturally consumes only a small part of a chapter, the aim of which is to stress the need of all three approaches to the study of mental illness: (1) psychological (including psychiatric); (2) physiological (including neurophysiological, electrophysiological, biochemical), and (3) social (including anthropological). The schizophrenia chapter presents no final evaluation of psychosurgery; it does present competent views, on the one hand, from those who feel that current and hoped-for developments in psychosurgery offer the best hope of abolishing the violent wards in mental hospitals and, on the other hand, from those who feel that, since surgical procedures do not yet rest upon comprehensive and exact knowledge of the brain tissue that is being ablated or the nerve pathway that is being severed, a physiological basis for psychosurgery has not yet been established.

Reading these two volumes is facilitated by the clear organization of the material and the lucid charm of the writing. As one of my colleagues on the Committee of Consultants put it, "The writing is of the best." While most of the reviews have naturally come from scientific and professional journals here and abroad, the late Waldemar Kaempffert of the New York *Times*, found the presentation "lucid enough for the layman and detailed enough for the scientist." The *New Yorker* recommended the volumes to the general reader as "a model of clarity, illumination, and hope."

I. S. Ravdin, Philadelphia

Surgery Illustrated

Splenectomy

JOHN L. MADDEN, M.D., New York

Comment

Splenectomy

William D. Holden, M.D., Cleveland

The principal hazard encountered in performing a splenectomy is hemorrhage. The operative procedure may be relatively simple or it may tax the patients and ingenuity of the surgeon to the utmost.

The type of incision is of great importance in facilitating technical maneuvers during the operation. The left paramedian incision (Plate I*A*) extending upward to the vicinity of the xiphoid process provides better exposure than either a transverse or subcostal incision (Plate I*B*). This extension is especially worth while because the densest peritoneal attachments of the spleen to the posterior parietal peritoneum are frequently at the upper pole. The gastrosplenic ligament can also be exposed and clamped most easily when the incision is extended upward as far as possible. When a splenorenal anastomosis is anticipated and considerable portacaval collateral channels exist, a combined thoracoabdominal incision (Plate I*B*) provides better exposure and minimizes the danger of bleeding. A combined incision is not ordinarily necessary, however, even when splenic venous hypertension exists if care is taken and the surgeon has had experience with this type of surgery.

With a paramedian incision the muscle preferably should be retracted laterally rather than split (Plate I*D*). Fewer anatomical relationships are disturbed, and trauma to the motor branches of the intercostal nerves supplying the rectus is reduced.

When a splenectomy is being performed for thrombocytopenia, the subcutaneous tissue in the incision oozes blood diffusely and continuously while the remainder of the incision through the abdominal wall is being made. This is apt to occur to a variable degree whether or not fresh whole blood or platelet suspensions are given just prior to the operation. This oozing ordinarily stops during the course of the operation and should not disconcert the operator.

After incising the peritoneum, the surgeon should not explore manually the peritoneal cavity of thrombocytopenic patients because of the likelihood of producing retroperitoneal ecchymoses which can assume significant proportions.

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This article is the second of four based on "Atlas of Technics in Surgery" by Dr. Madden, to be published in September, 1957, by Appleton-Century-Crofts, New York.

Because of difficult exposure, it is not always possible to incise the lienorenal ligament, which in essence is the posterior parietal peritoneum as it comes medially and anteriorly over the spleen (Plate 1*G*). With experience the retroperitoneal space may be entered with the tip of a finger and the peritoneum separated bluntly. It is important not to place this peritoneal opening too close to the spleen, in order to avoid stripping the peritoneum from the splenic tissue, with resulting bleeding.

The gradual and gentle separation (Plate 1*H*) of the splenic pedicle from other retroperitoneal tissues is perhaps the most important maneuver in the operation. A few extra minutes here may save considerable blood loss and many minutes of frustrating effort to control the bleeding. After completion of this manipulation, ordinarily the spleen will be sufficiently mobile that the remainder of the operation can be done under direct vision. Occasionally, however, the spleen cannot be completely mobilized because of insufficient length and elasticity of the splenic vessels. In these circumstances it is worth while to place a sponge or hernial tape loosely about the pedicle so that any sudden hemorrhage can be controlled promptly. If it becomes necessary to tighten this hemostatic tourniquet, the tail of the pancreas may be included in it. Temporary constriction of the pancreas, however, does no permanent damage.

(*Comment continued on page 638*)

PLATE I

A, a left rectus paramedian, muscle-splitting incision, the one preferred, is depicted. In this patient the spleen was huge and produced a visible bulge to the left side of the anterior abdominal wall.

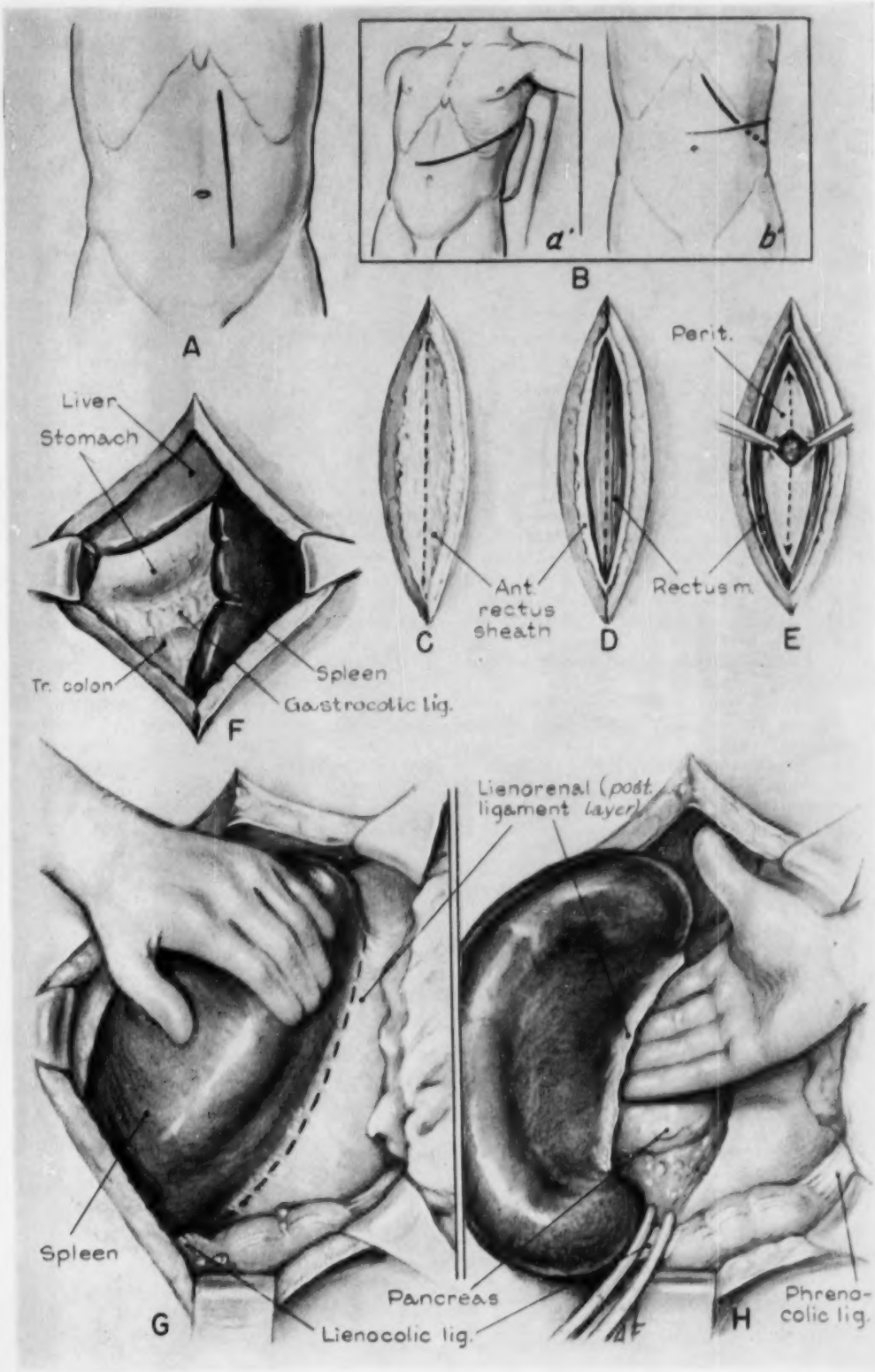
B, alternate incisions which may be used: (a^1) Combined abdominothoracic. (b^1) Transverse and subcostal incisions with the dotted line to show the extension of the subcostal incision if desired.

C, *D*, *E*, dotted outlines to indicate the incisions through the anterior rectus sheath, the left rectus muscle, and the peritoneum respectively.

F, the peritoneal cavity is entered, and the wound margins are retracted to show the notched border of the enlarged spleen and its related structures.

G, by careful manual manipulation the spleen is displaced medially, and the incision in the layer of peritoneum which forms the posterior layer of the lienorenal ligament is in dotted outline. Ordinarily this layer is avascular. However, in some instances of hypersplenism, particularly so-called Banti's syndrome, its marked vascularity necessitates the application of clamps prior to division.

H, by digital manipulation in the retroperitoneal tissue plane the mobilization of the spleen is continued. The lienocolic ligament is shown doubly clamped before it is severed.


A
a
b
B
Perit.
Ant. rectus sheath
Rectus m.
C
D
E
Liver
Stomach
Tr. colon
Spleen
Gastrocolic lig.
F
Lienorenal (post. ligament layer)
Spleen
Pancreas
Lienocolic lig.
G
H
Phrenocolic lig.

The splenic artery and vein may be brittle or friable, especially in elderly patients. In these circumstances, no effort should be made to separate the vein from the artery for individual ligation. Because of the danger of tearing the vessels, the application of clamps (Plate III*L*) prior to ligation is not always desirable; instead, two 00 silk ligatures passed around the main vessels are less traumatic and hazardous.

Fortunately, most accessory spleens (Plate III*L*) will be encountered around the hilus of the spleen. Throughout the operation, however, the surgeon must be aware of the possibility of finding them elsewhere, such as along the course of the splenic vessels, in the gastrocolic omentum, or even in the tail of the pancreas.

(*Comment continued on page 640*)

PLATE II

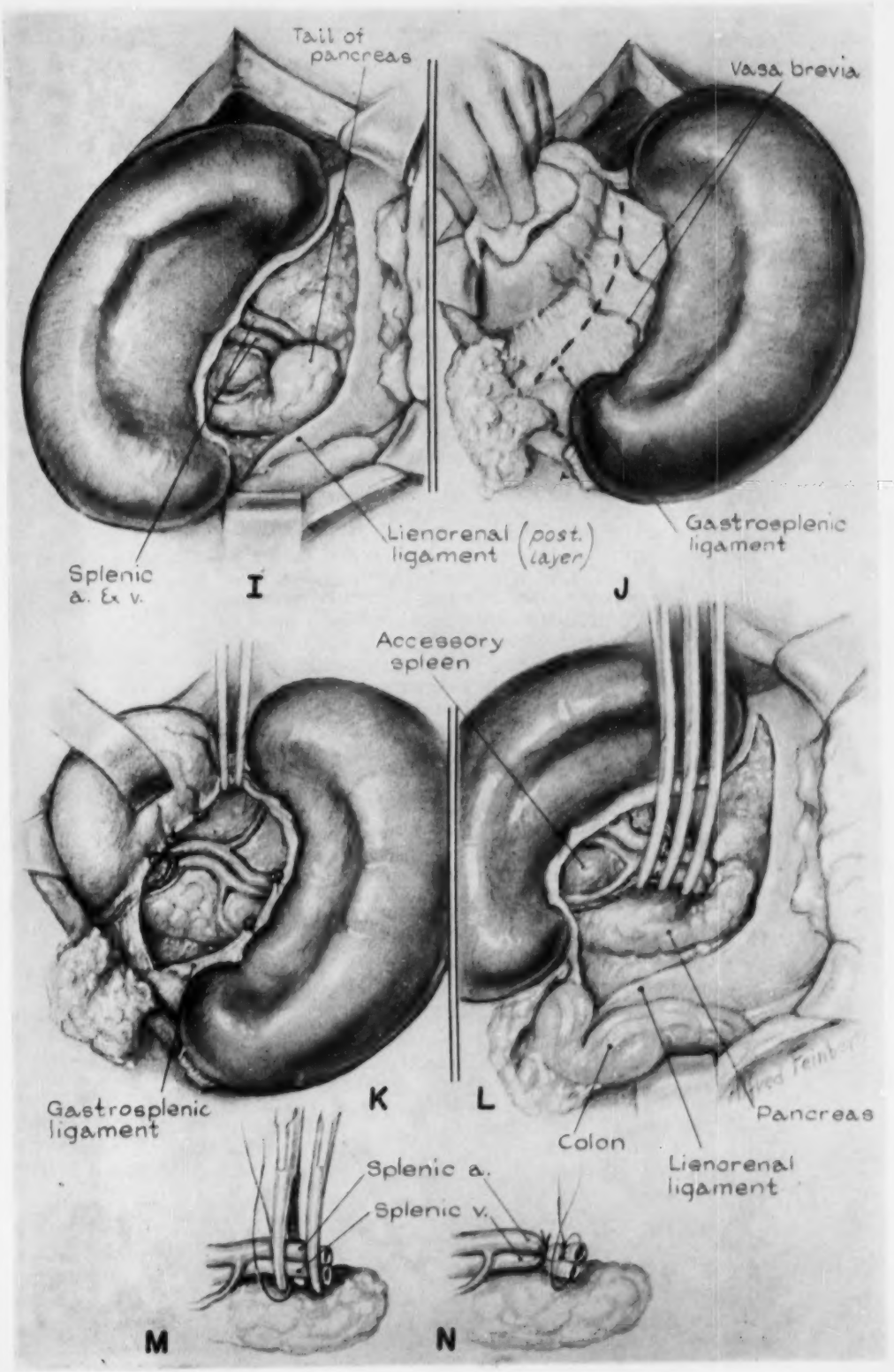
I, the mobilization posteriorly is completed and the spleen is easily displaced upward into the abdominal incision. The posterior aspect of the splenic pedicle and its relation to the tail of the pancreas is demonstrated. In the dissection posteriorly, particular precaution should be taken to avoid injury to the tail of the pancreas, which is frequently in close approximation to the hilum of the spleen and its vascular pedicle.

J, the spleen is withdrawn through the incision and rotated laterally onto the anterior abdominal wall. Traction upward on the greater curvature of the stomach is maintained, and the line of division of the anterior layer of the gastrosplenic ligament and its contained vasa brevia are shown in dotted outline.

K, the division of the gastrosplenic ligament is almost completed and the anterior aspect of the splenic pedicle is visible. The uppermost part of the anterior layer of the gastrosplenic ligament is relatively short. Accordingly, in the application of clamps to this ligament one must be careful to avoid injury to the greater curvature of the stomach and the superior pole of the spleen. Furthermore, the uppermost part of the gastrosplenic ligament contains one of the vasa brevia. An avulsion tear of this vessel may be a frequent cause of troublesome hemorrhage during the performance of splenectomy.

L, the spleen is completely mobilized, and its vascular pedicle, which is contained within the posterior layer of the gastrosplenic ligament and the anterior layer of the lienorenal ligament, is triply clamped prior to its division between the two distal clamps. In the application of the clamps to the splenic pedicle injury to the tail of the pancreas should be avoided. If preferred, triple ligation in continuity without the use of clamps may be performed. The center ligature is of the transfixion type distal to which the pedicle is severed. The artery and vein may be ligated either separately or as a unit structure. This method is used frequently because of the friability of the vessels. In every splenectomy performed for hypersplenism a diligent search is always made for accessory splenic nodules, one of which is depicted in juxtaposition to the hilum. Removal of all such nodules is mandatory.

M, *N*, the application of a proximal ligature and distal transfixion suture ligature of silk (00) respectively to the vascular pedicle following the removal of the spleen.


Tail of pancreas
Vasa brevia
Splenic a. & v.
Lienorenal ligament (post. layer)
Gastroeplenic ligament
I
J
Accessory spleen
Gastrosplenic ligament
K
L
Pancreas
Colon
Lienorenal ligament
Splenic a.
Splenic v.
M
N

Preliminary double ligation in continuity of the splenic vessels (Plate III*T*), to facilitate the removal of a densely adherent spleen, can be of value. When a previous inflammatory process has been present along the upper border of the pancreas, it is not always easy to dissect the vessels out. Ligation must be done distal to the origin of the left gastroepiploic artery; otherwise, little is gained by this maneuver.

An essential feature of this operation is careful inspection of the splenic pedicle and the denuded retroperitoneal space for bleeding, after the spleen has been removed. It is much easier to find a small bleeding vessel, and to either ligate or suture it, at this time than several hours later.

PLATE III

O, the operation is completed, and the occluded vascular pedicle of the spleen and its related structures are demonstrated.

P, the anatomic relations of the intraperitoneal viscera prior to wound closure.

Q, *R*, *S*, layer closure of the abdominal incision using interrupted mattress sutures of silk (00) for the peritoneum, interrupted sutures of silk (00) for the fascia, and interrupted sutures of silk (000) for the skin.

T, this insert depicts the preliminary double ligation in continuity of the splenic artery as advocated by the late A. O. Singleton as a technical aid in the removal of a large or densely adherent spleen. The lesser sac is entered through an opening in the gastrocolic ligament, and the splenic artery is identified by inspection and palpation as it courses along the superior border of the pancreas. The peritoneum of the posterior wall of the lesser sac overlying the pancreas is divided and the artery is ligated in continuity with two ligatures of silk (00).

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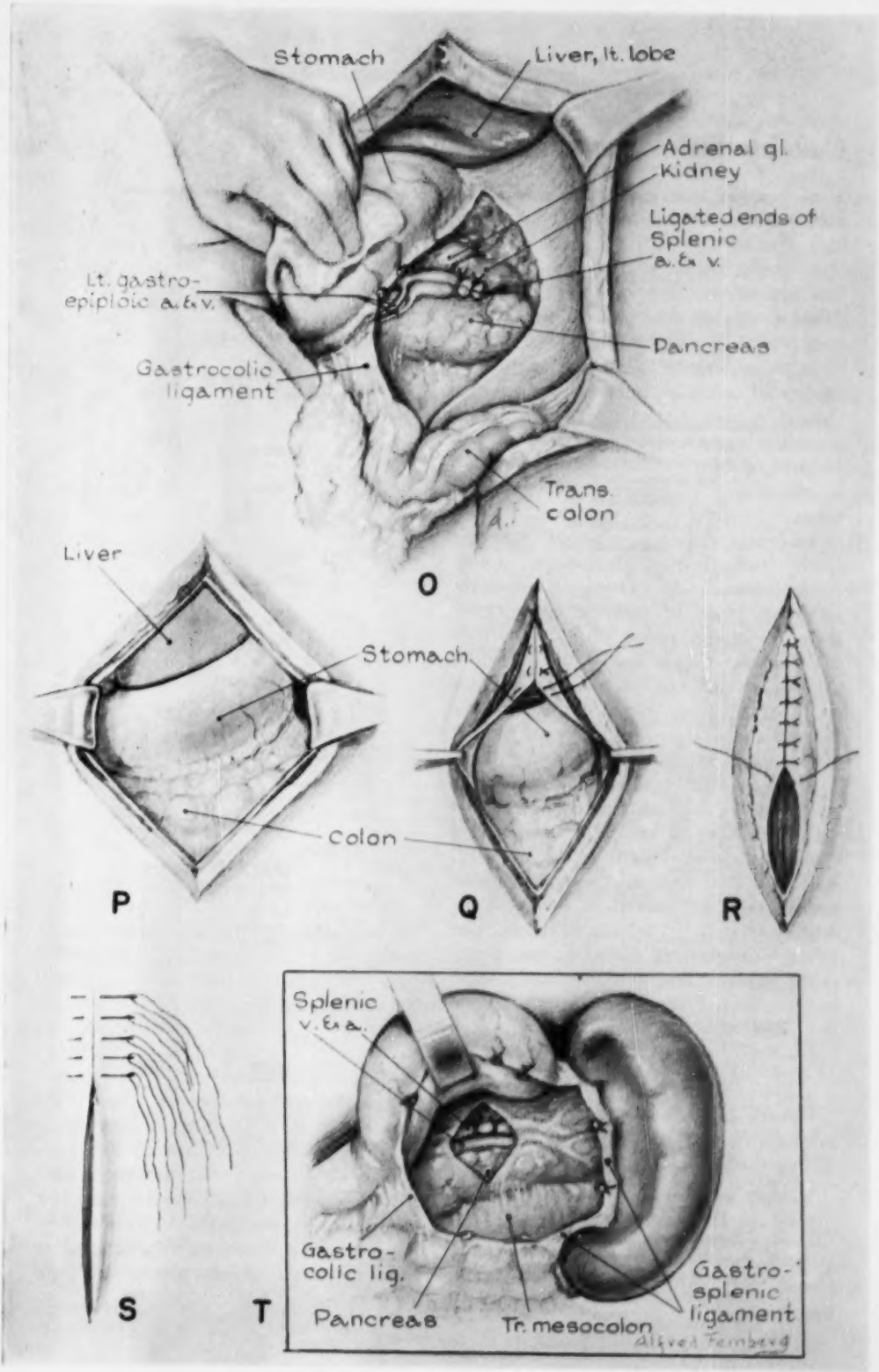

Stomach
Liver, lt. lobe
Adrenal gl.
Kidney
Ligated ends of Splenic a. & v.
Lt. gastro-epiploic a. & v.
Pancreas
Gastrocolic ligament
Trans. colon
O
Liver
Stomach
Colon
P
Q
R
S
T
Splenic v. & a.
Gastro-colic lig.
Pancreas
Tr. mesocolon
Gastro-splenic ligament
Alfred Fernberg

Carcinoma of the Lung

ALTON OCHSNER, M.D.; R. J. SCHRAMEL, M.D.; JOHN BLALOCK, M.D.; J. H. KEELING, M.D., and JACK HALEY, M.D., New Orleans

Introduction

Since 1934 we have seen 1360 patients with a definite clinical diagnosis of carcinoma of the lung on the Tulane Services at Charity Hospital of Louisiana and at the Ochsner Clinic. Analysis of these cases is presented to emphasize the common clinical features of this serious visceral tumor. It is increasingly recognized that there is considerable variability in the characteristics of malignant disease as reported from different institutions. This usually results from differences in methods of reporting or from factors of selection operating in these institutions rather than from variations in the disease itself. We therefore believe that information derived from a study of all cases seen in a large public hospital and a large private hospital serving the same area should be generally applicable.

An increasing incidence of occurrence of this tumor is being reported throughout the civilized world. Survival rates remain distressingly low. This is all the more discouraging in view of the tremendous public and professional interest in this problem. Nonetheless, it is our opinion that the fullest utilization of diagnostic and therapeutic methods now available would result in a substantial increase in survival beyond five years.

Results

Figures 1-3: Carcinoma of the lung is predominantly a disease of men between the ages of 50 and 70 years. The pronounced difference in racial incidence in this series is a reflection of the largely white patient admissions at the Ochsner Clinic. At Charity Hospital in New Orleans, where white and Negro patients are seen in equal

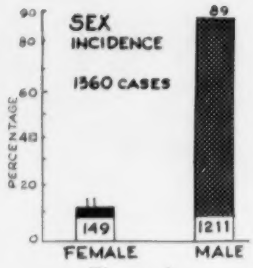


Figure 1

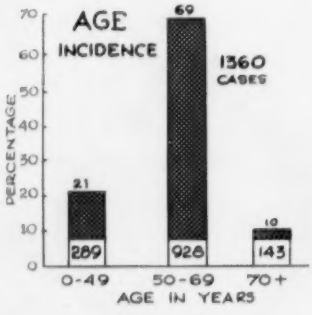


Figure 2

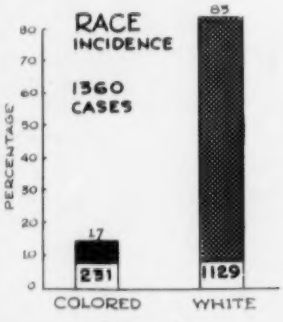


Figure 3

Received for publication Oct. 1, 1956.

From the Departments of Surgery, Ochsner Clinic and Tulane Medical School, and Charity Hospital of Louisiana. Fellow of the American Cancer Society (Dr. Schramel).

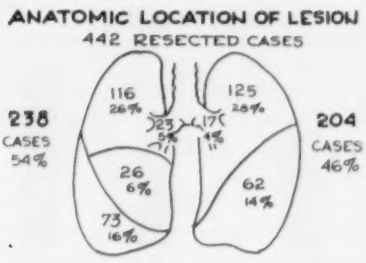
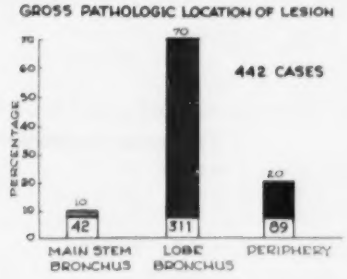


Figure 4



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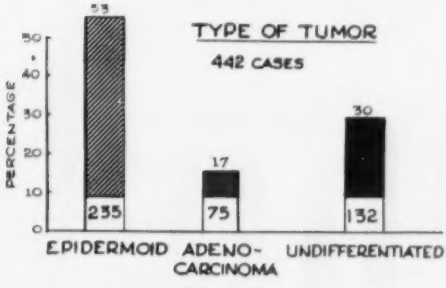


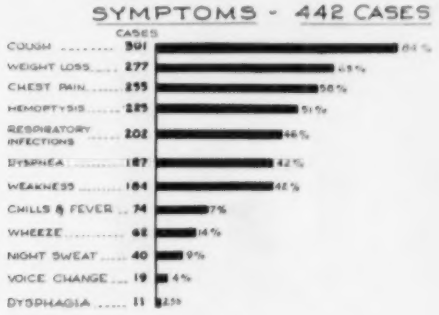
Figure 6

numbers, there is nonetheless a definite difference in racial incidence. There were 1020 cases per 100,000 adult white male admissions and 597 cases among 100,000 adult Negro male admissions between 1948 and 1955.

Figures 4-6: The tumors arose predominantly from lobar and segmental bronchi of the upper lobes of the lung. These findings were derived from careful study of resected specimens.

Figures 7-9: Only 24 patients in the group having resection were asymptomatic. In only 16% of patients having resection was the diagnosis made by cytologic examination of the sputum. Many patients in this series were seen before use of this diagnostic procedure was adopted here. Positive results were obtained in 35% of the patients having resection in whom cytologic examination was done.

Figures 10-15: The classification of curative and palliative resections is a surgical pathologic one, indicating, respectively, resections for tumor confined to the lung and those including metastatic growth or direct extensions beyond the lung. The ideal treat-



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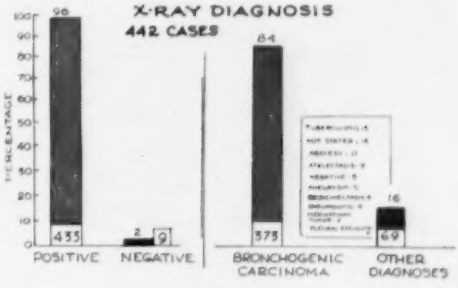

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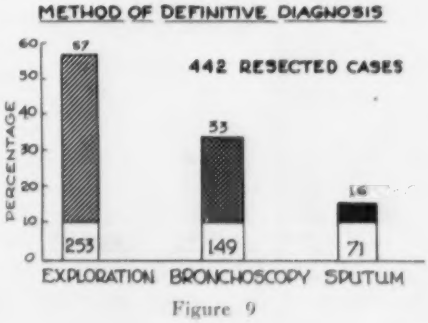

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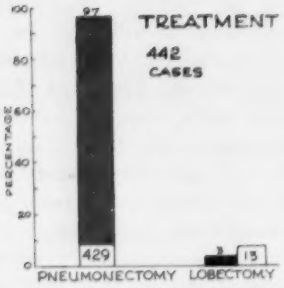
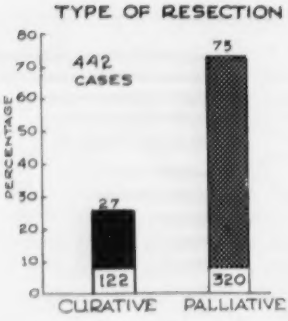


Figure 10



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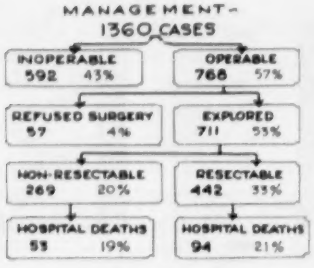

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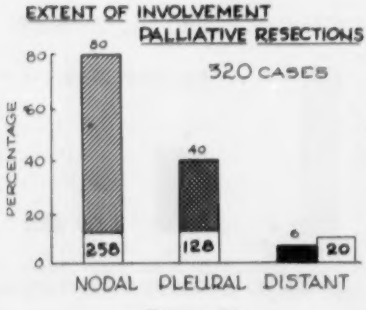

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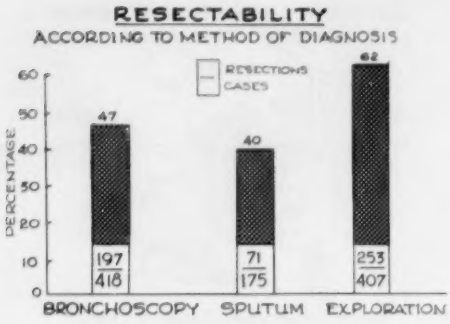

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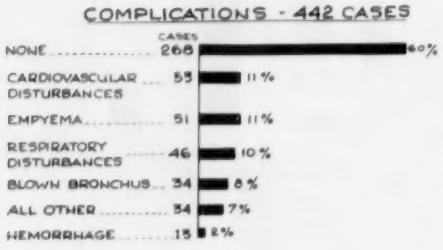

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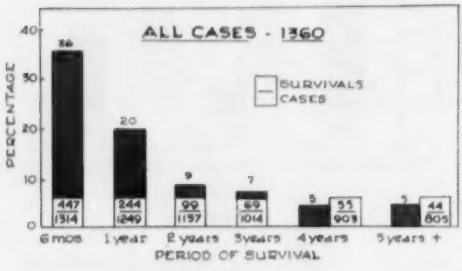

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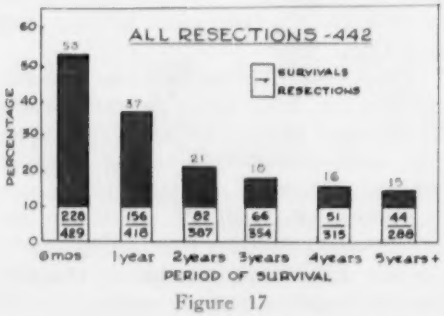
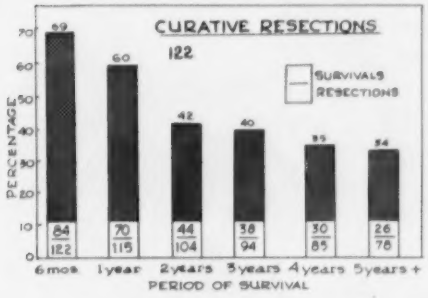


Figure 17

ment of bronchogenic cancer is radical pneumonectomy with en bloc excision of the mediastinal lymph nodes. In patients with tumors that extend beyond the lung (in 80% the mediastinal nodes were involved, and in 40% the tumors involved the parietes), pneumonectomy is still justifiable and, although it is considered a palliative procedure, it is frequently curative. Only 53% of the tumors in our series were operable, and in only 33% was the lung resectable.

The 20 patients with distant involvement were persons who had died during the postoperative period, and at autopsy distant metastases were found. We do not operate on patients with known extension beyond the thorax.

Figures 16-18: These cases were followed through Dec. 31, 1955. In the group of palliative resections there were 18 five-year survivors, or a five-year survival rate of 8% for patients with known extension beyond the lung who had resection.



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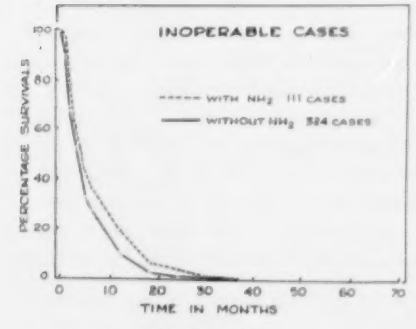

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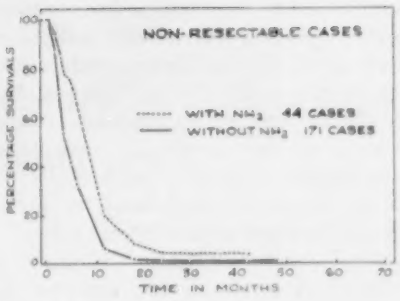

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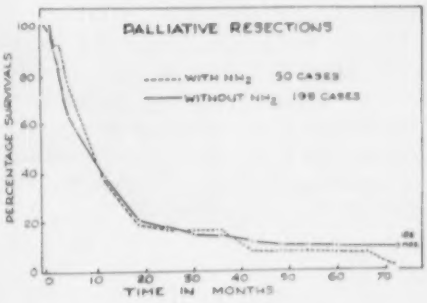

Figure 21

Figures 19-21: Patients who have not had a curative resection receive repeated courses of mechlorethamine hydrochloride (nitrogen mustard), which we believe to be of considerable palliative benefit. Effect of this therapy on survival is difficult to determine, but there is some increased short-term survival of patients with operable but nonresectable tumors.

Conclusions

It is readily apparent that if survival rates are to be improved, patients must have adequate surgical excision while the disease is confined to the lung. Since practically all these lesions produce an abnormality which can be detected radiologically, our best method of discovering cases is widespread use of roentgenography of the chest in the group of persons who are maximally susceptible to bronchogenic carcinoma, that is, men more than 40 years of age who are heavy cigarette smokers. Our best method of diagnosing curable cases is surgical ex-

ploration. The appearance of symptoms, positive bronchoscopic findings, and positive results of sputum examination seem to indicate an unfavorable but not hopeless situation. This form of management (surgical exploration for otherwise undiagnosed abnormalities detected radiologically) is having increasing application at present through discovery of many "coin lesions" in radiologic surveys. Early reports[1,2] of series of these lesions are somewhat disappointing, but optimum application of surgical treatment generally has not been realized.

Despite the growing awareness of the great influence that the biologic characteristics of a tumor exert on prognosis, the basis of our plan of management remains early diagnosis and early adequate excision. An important corollary is that many tumors of known long duration will be still confined to the lung and potentially curable. Treatment should not be withheld except for known extrathoracic disease and inability of the patient to tolerate the contemplated procedure.

Ochsner Foundation Hospital, 1516 Jefferson Highway (21).

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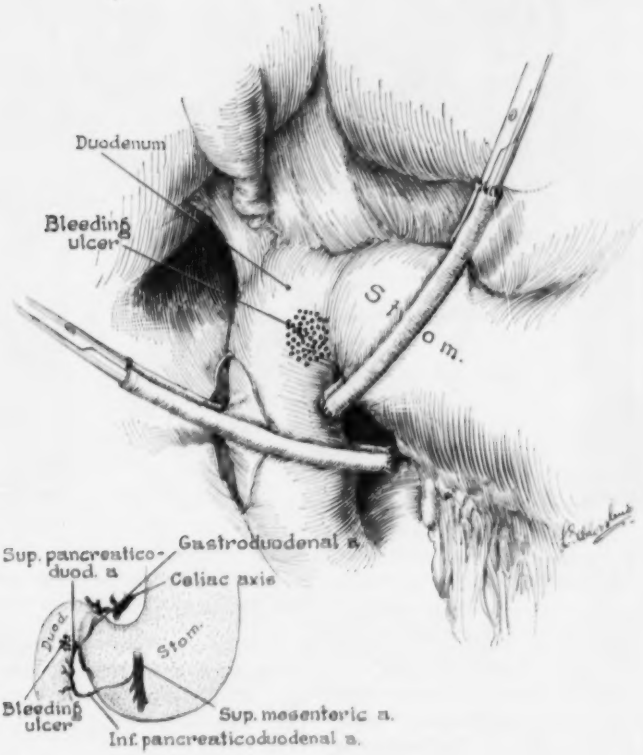
A Method for the Immediate Control of Hemorrhage from Duodenal Ulcer at Operation

I. RIDGEWAY TRIMBLE, M.D., Baltimore

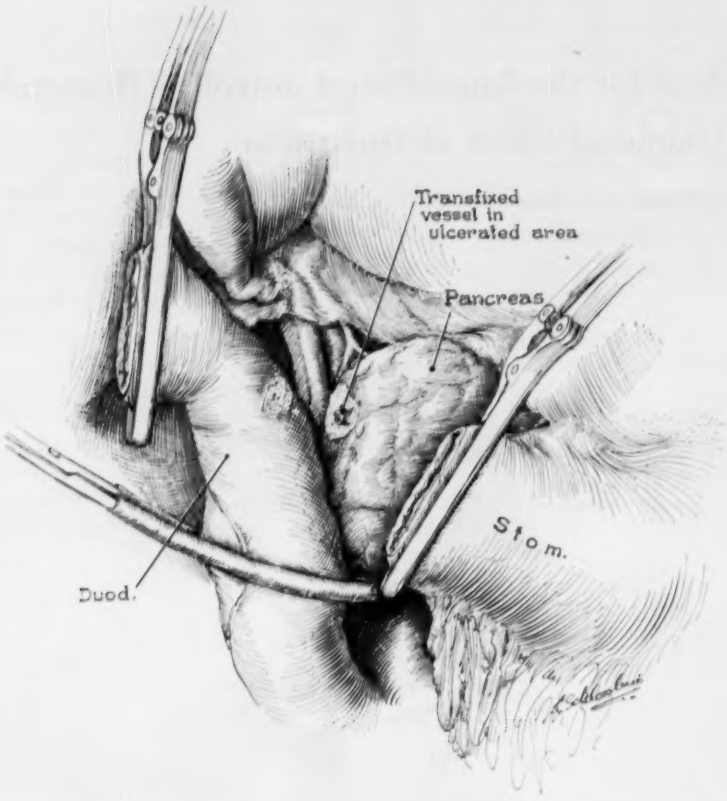


Bleeding from a duodenal ulcer almost always arises from either the superior or the inferior pancreaticoduodenal artery as they enter the scarred, noncontractile base of the ulcer. When an emergency operation is undertaken for continuing bleeding, the hemorrhage into the bowel may be so severe as even to be fatal while the operation is in progress, before the ulcerated portion of the bowel can be dissected free from the open, bleeding vessel, or even before the bleeding vessel can be transfixed.

A method is presented which has proved of great value in controlling the hemorrhage immediately after the laparotomy incision has been made. This method consists in applying a rubber- or linen-shod clamp across the duodenum just distal to the area of ulceration and another similar clamp across the stomach just proximal to the pylorus.

Submitted for publication July 24, 1956.

From the Department of Surgery of The Johns Hopkins Hospital and Medical School.

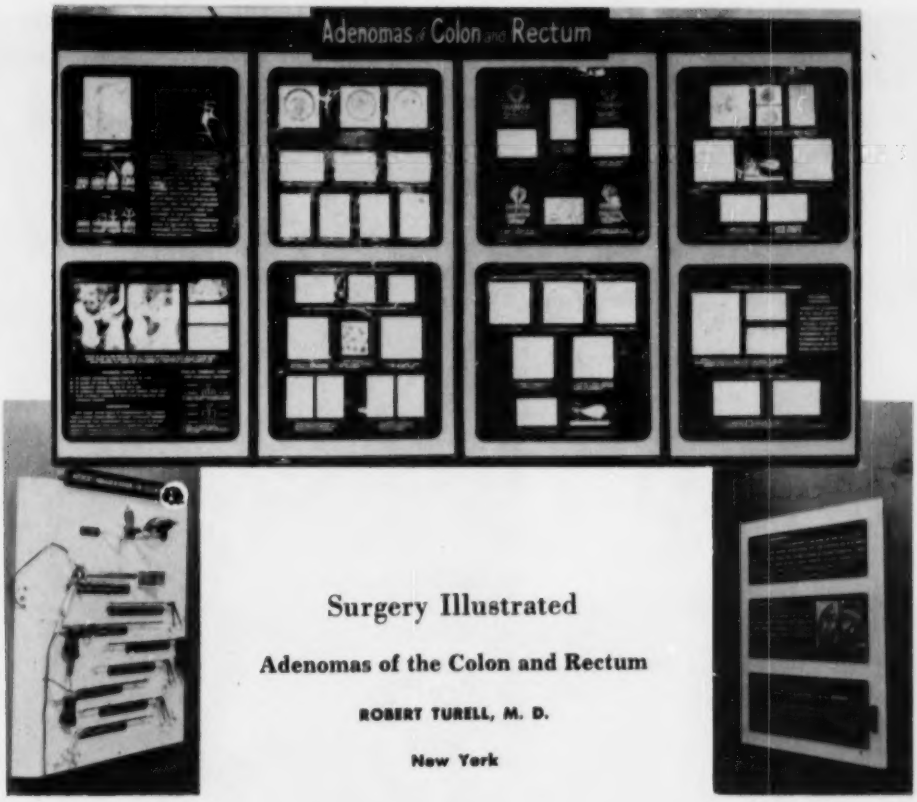


Any further hemorrhage which may arise from the bleeding vessel is then confined to this short segment of distal stomach and proximal duodenum. Besides limiting the space into which hemorrhage may take place, the increase in intraluminary pressure in the segment produced by the action of the two clamps acts as a tamponade to an open blood vessel in which there may be a loose clot. Dissection of the involved segment of duodenum and of the distal stomach may then be undertaken without undue haste and without the compulsion attendant when an artery is bleeding or is thought to be bleeding freely into the open duodenum and stomach.

If only transfixion of the bleeding vessel is decided upon, the duodenum can be opened between the two rubber- or linen-shod clamps and then resutured.

If, as is usually the case, a subtotal gastrectomy is decided upon, a Payr type set of clamps is substituted for the proximal rubber-shod clamp in order to hold more firmly those portions of the stomach and duodenum which are to be resected.

2947 St. Paul St. (18).



Surgery Illustrated

Adenomas of the Colon and Rectum

ROBERT TURELL, M. D.

New York

This exhibit is based primarily on personal experience with adenomas of the colon and rectum. Although some aspects of this problem have no ready solution, a relatively uniform pattern is nevertheless discernible.

A special word about biopsy of adenomas: We are against fractional biopsy because the character of the interior of the body or the base of the lesion is not usually revealed. We practice "total biopsy," or the removal of the entire polyp at its base in one piece or in several large segments, which has real diagnostic and at the same time therapeutic value. We maintain great reservations about any diagnosis in adenomas that is based on frozen section technique, since the best pathologists can be deceived in both directions.

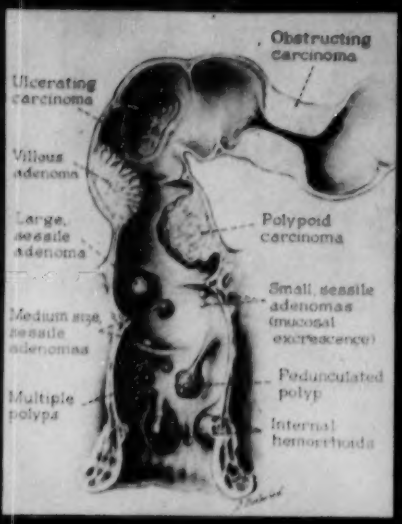
The criteria for the early diagnosis of early cancer in adenomas, particularly that of the noninvasive variety, differ enormously with the experience and perhaps the philosophy of the pathologist. In general, a diagnosis of invasive cancer should be made emphatically unequivocal. Equivocation causes or augments fear or cancerphobia on the part of the patient, and frustration and inaction on the part of the clinician.

We believe that while colorectal adenomas have a dangerous propensity to undergo malignant transformation, some may remain benign. However, since there are no gross or microscopic criteria that will enable the proctologic surgeon or the pathologist to predict a benign course for a given adenoma, or to foretell when malignant transformation might be expected, we extirpate all colorectal adenomas upon recognition as a matter of good prophylaxis, even if only a minority of colorectal adenomas do become cancers.

The ideal treatment of multiple (more than three) discrete benign adenomas is probably subtotal colectomy and an anastomosis of the ileum to the upper rectum or the lowest portion of the sigmoid colon, or extirpation through extended colotomy incisions.

In an experience of many hundreds of electrocoagulations of primary and recurrent adenomas, we have encountered a 5% incidence of some bleeding within the first 24 hours of coagulation and a somewhat lower incidence of secondary bleeding (five or more days after coagulation) following the use of the snare. Perforations have never occurred in

TYPES OF ADENOMAS



(NOTE OTHER LESIONS THAT PRODUCE BLEEDING)

GENESIS OF ADENOMAS

CLASSIFICATION OF ADENOMAS

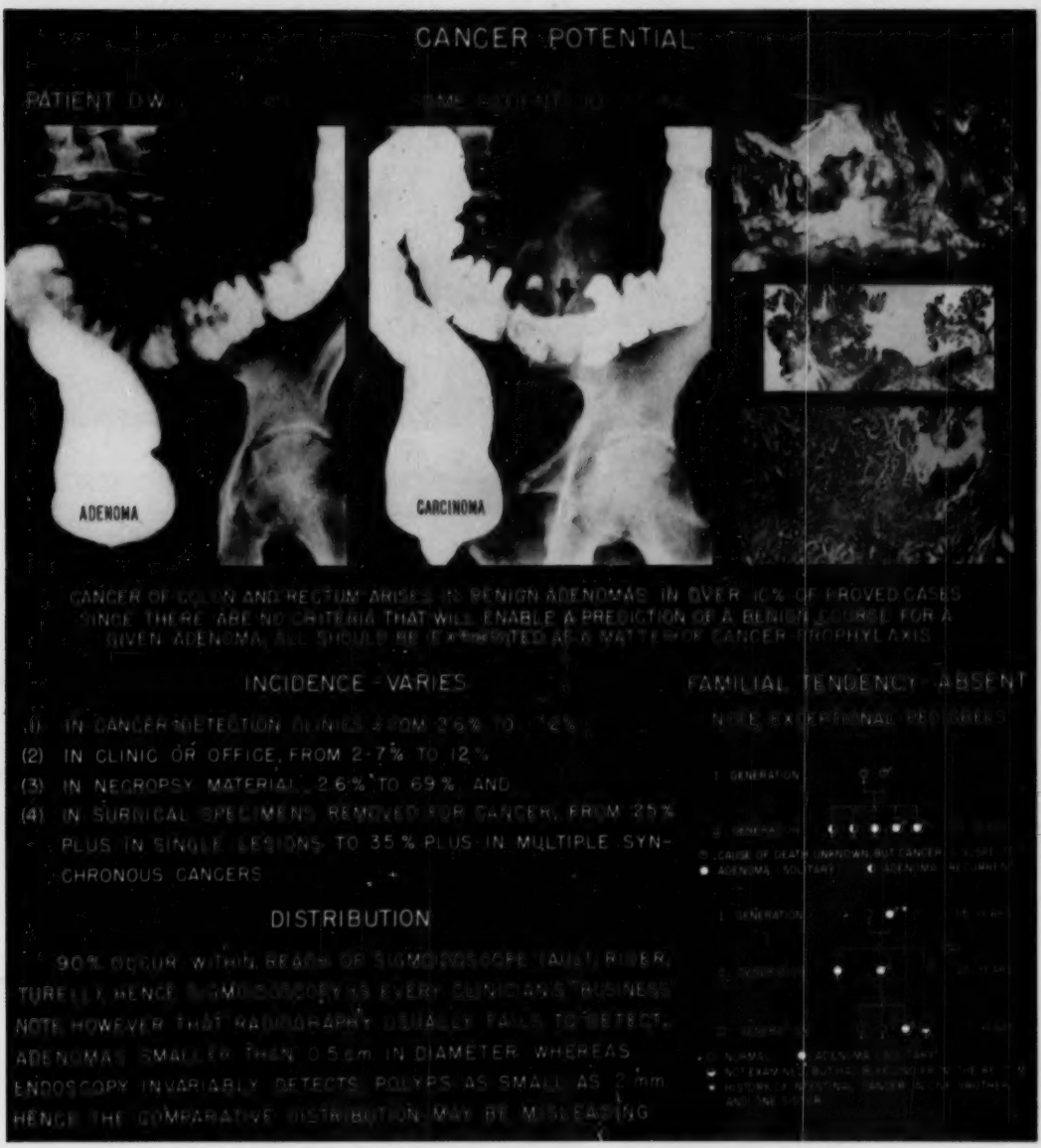
A COMPLEX CLASSIFICATION IS UNDESIRABLE (AND UNJUSTIFIED)

1. SINGLE OR MULTIPLE (SCATTERED) — ACQUIRED / FAMILIAL
2. PEDUNCULATE OR SESSILE
3. SMOOTH OR VILLOUS
4. BENIGN OR MALIGNANT — NONINVASIVE / INVASIVE

THE DETERMINING BOUNDARY OF INVASION IS THE *MUSCULARIS MUCOSAE*. INVASION THROUGH THE MUSCULARIS MUCOSAE IS REGARDED AS FRANK *CANCER*. CANCER CELLS MAY FORTUITOUSLY ENTER THE BLOOD OR LYMPHATIC VESSELS OF A STALK AND CAUSE REGIONAL OR DISTANT METASTASES (EMBOLIC ROUTE) WITHOUT INVASION OF THE PEDICLE OR THE MUSCULARIS MUCOSAE. ONLY FEW SUCH INSTANCES HAVE BEEN REPORTED; NONE HAS OCCURRED IN OUR EXPERIENCE.

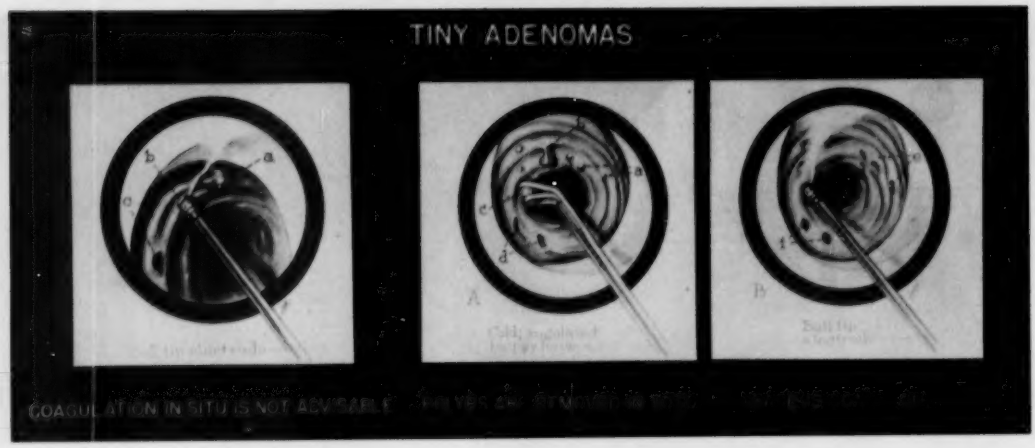
THE CONCEPT OF A "PRECANCEROUS" LESION IS BELIEVED TO INDICATE AN INCREASED STATISTICAL PROBABILITY OF DEVELOPING CANCER.

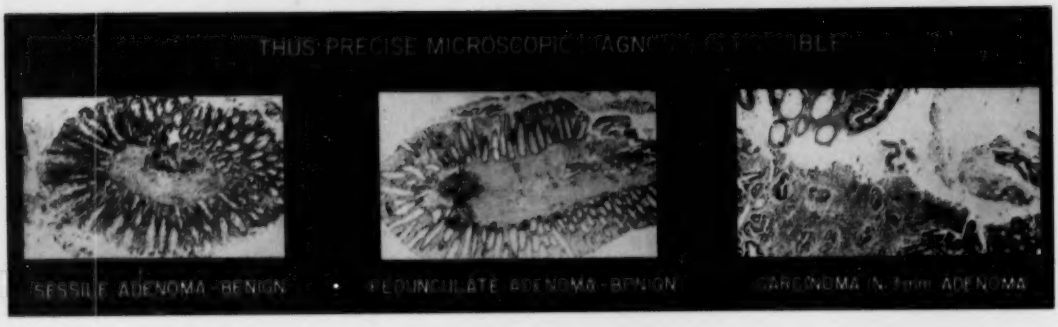
our hands, in spite of the fact that the snare is employed as far as the sigmoidoscope will reach, provided the lesion can be visualized well enough for the safe looping of the stalk. In a questionable case laparotomy failed to reveal the tear but showed edema of the

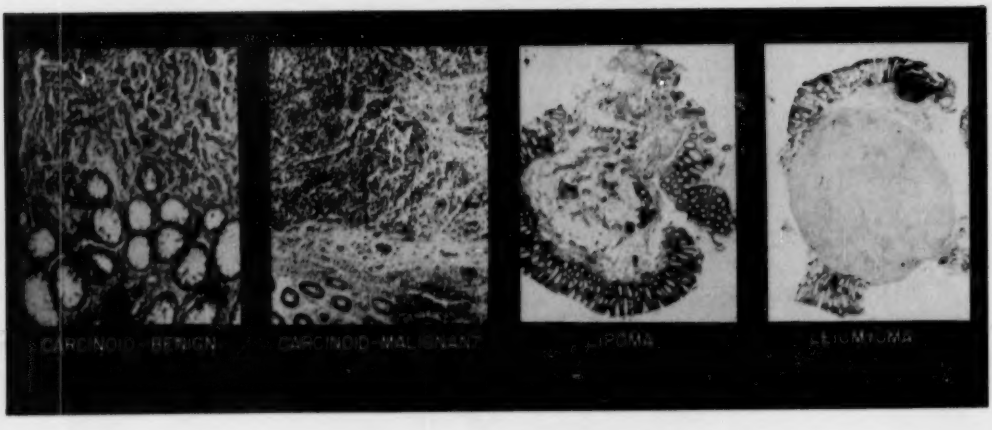

CANCER POTENTIAL
ADENOMA
CARCINOMA
INCIDENCE - VARIES
(1) IN CANCER DETECTION CLINICS FROM 3.6% TO 12%
(2) IN CLINIC OR OFFICE, FROM 2-7% TO 12%
(3) IN NECROPSY MATERIAL, 2.6% TO 69% AND
(4) IN SURGICAL SPECIMENS REMOVED FOR CANCER, FROM 25% PLUS IN SINGLE LESIONS TO 35% PLUS IN MULTIPLE SYNCHRONOUS CANCERS
DISTRIBUTION
FAMILIAL TENDENCY - ABSENT

bowel above the rectosigmoid. A similar experience occurred on Sept. 14, 1955, in an obese psychoneurotic woman with hypertensive cardiovascular nephritic disease. She recovered without laparotomy.

Gas explosions with resultant perforation of the gut during coagulation of adenomas, a potential complication of variable seriousness, have never occurred in our experience.

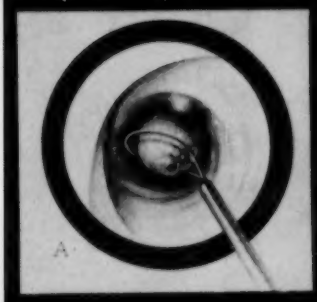

TINY ADENOMAS
COAGULATION IN SITU IS NOT ADVISABLE


SESSILE ADENOMA - BENIGN
PEDUNCULATE ADENOMA - BENIGN
CARCINOMA IN from ADENOMA


CARCINOID - BENIGN
CARCINOID - MALIGNANT
LIPOMA
FIBROMYOMA

PEDUNCULATE ADENOMAS

BENIGN AND NONINVASIVE MALIGNANT LESIONS ARE REMOVED AT BASE WITH SNARE



LOOPING OF POLYP

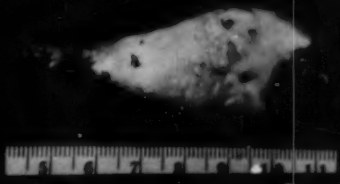
STRANGULATION OF STALK

COAGULATION OF RESIDUAL PEDICLE

TRACTION OF ADENOMA WHEN LOOPING IS DIFFICULT.

CLAMPING OF STALK, EXCISION OF BODY AND COAGULATION WHEN LOOPING IS IMPOSSIBLE

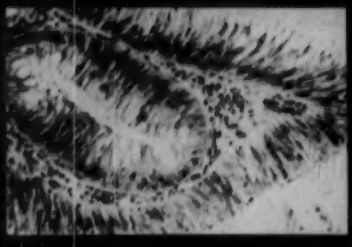
GROSS SPECIMEN AFTER SNARING



FIBROEPITHELIAL POLYP NOT TO BE CONFUSED WITH ADENOMATOUS POLYP

PEDUNCULATE ADENOMAS

A

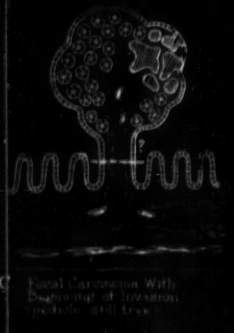


BENIGN

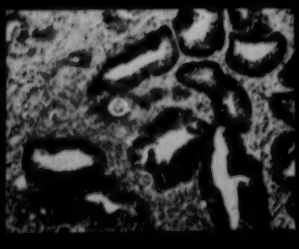
BENIGN AND NONINVASIVE MALIGNANCY IN SAME SPECIMEN

B Focal Carcinoma W... Invasion

NONINVASIVE MALIGNANCY STALK UNINVOLVED



C Focal Carcinoma With Beginning of Invasion...

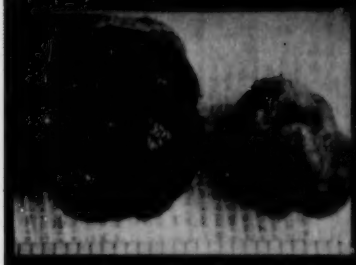


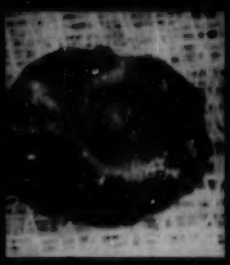
MALIGNANT INVASION OF STALK NEAR BODY OF POLYP SNARING (P...

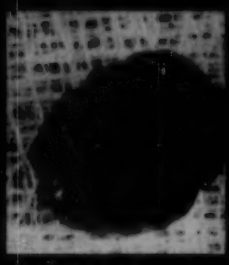
D

INVOLVEMENT OF STALK AND MUSCULARIS MUCOSAE RESECTION

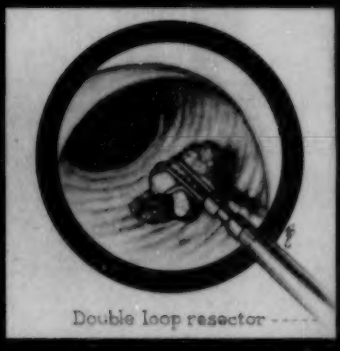
SESSILE (SMOOTH OR VILLOUS) ADENOMAS



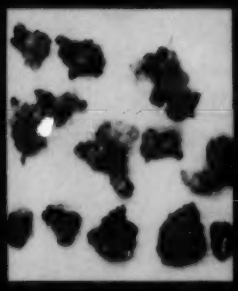




SMALL AND MEDIUM-SIZED LESIONS REMOVED WITH ELECTROTHERMIC SNARE

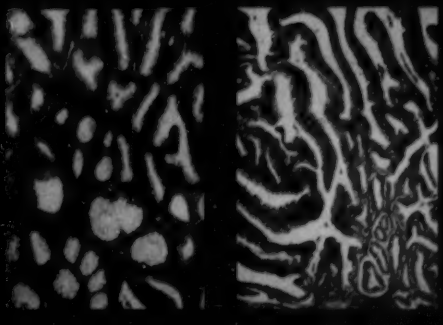


REMOVAL OF LARGE LESION WITH DOUBLE LOOP RESECTOR

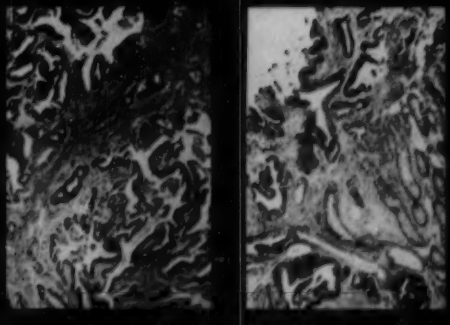


GROSS FRAGMENTS OF EXCISED TISSUE SUITABLE FOR MICROSCOPY

REMOVAL OF LARGE LESION AND RECTAL VALVE

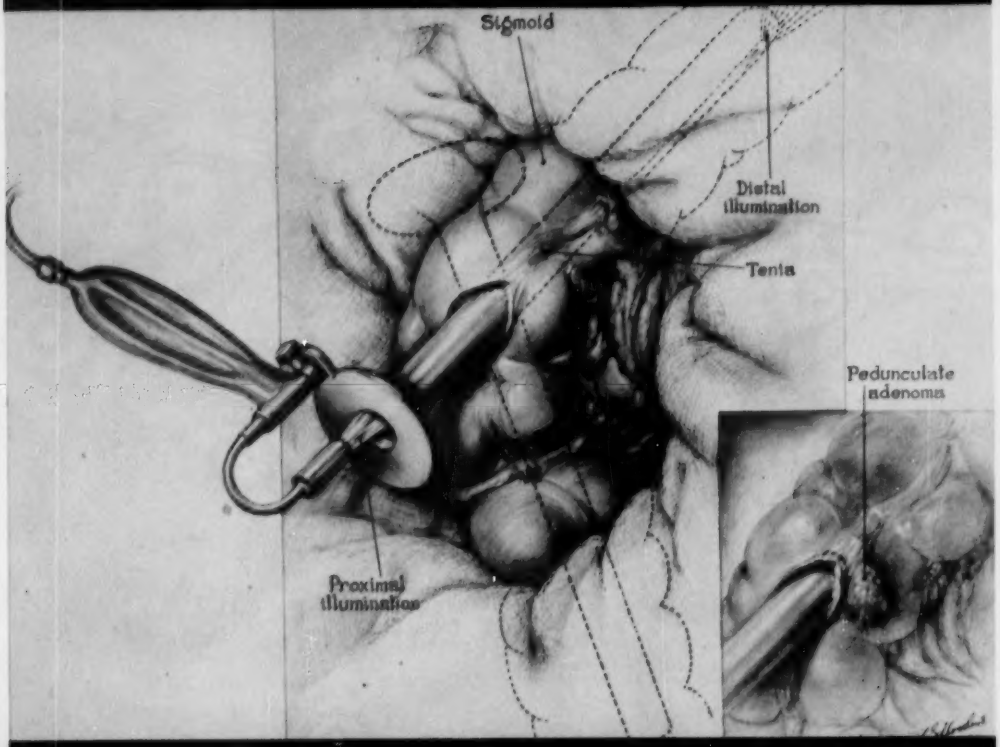


MICROSCOPIC APPEARANCE OF BENIGN SMOOTH ADENOMA AND BENIGN VILLOUS ADENOMA

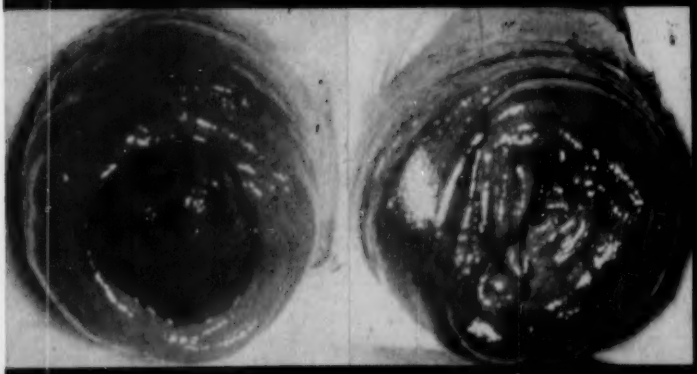


MICROSCOPIC DETECTION OF INVASIVE MALIGNANCY IN A VILLOUS ADENOMA

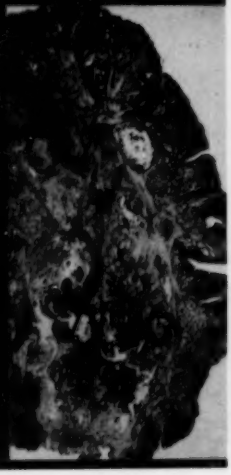
POLYPECTOMY THROUGH COLOTOMY FOR BENIGN PEDUNCULATE ADENOMAS

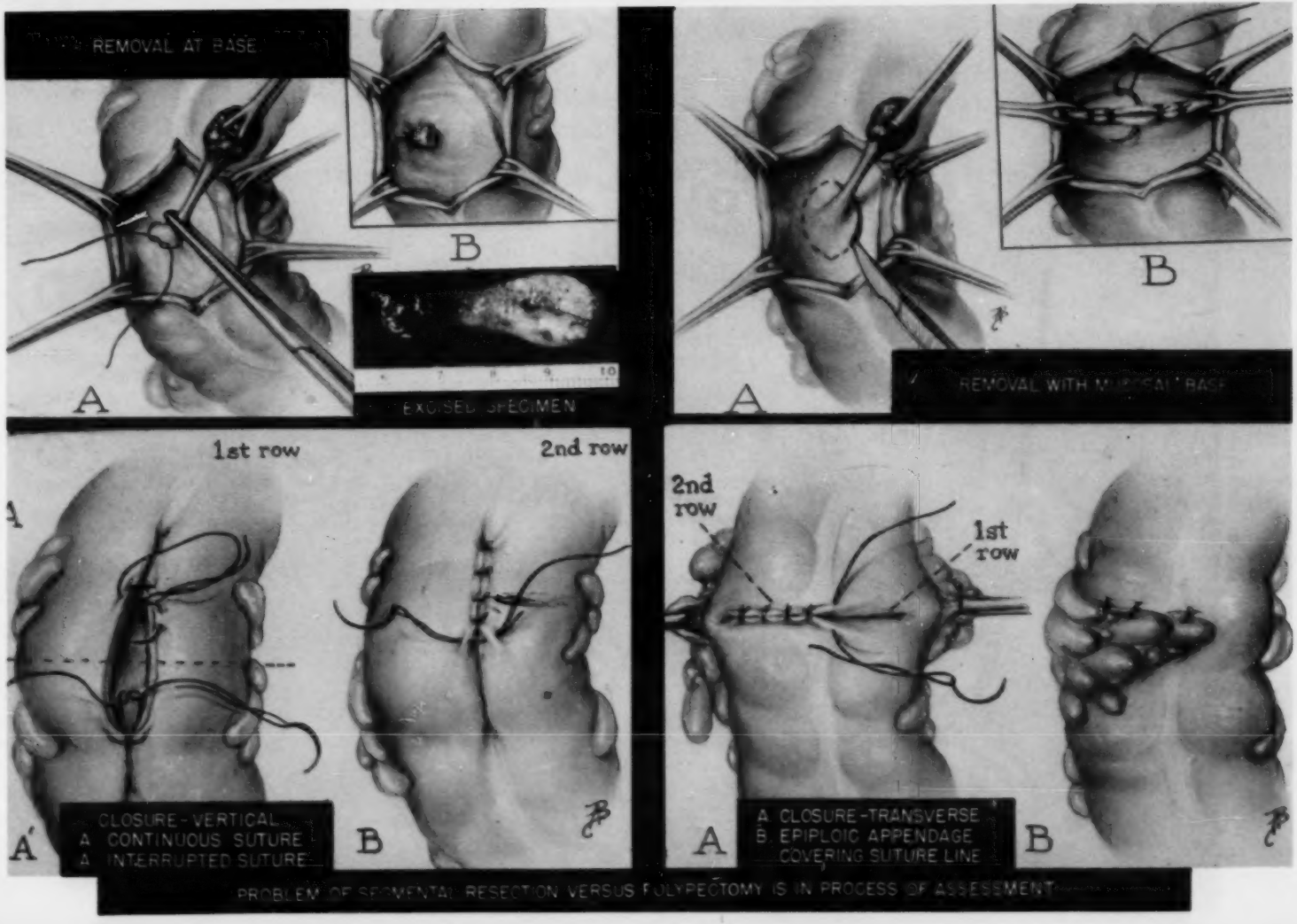


ENDOSCOPY AT TIME OF COLOTOMY (OR RESECTION)

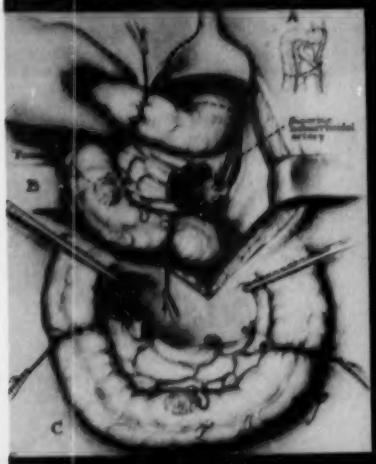


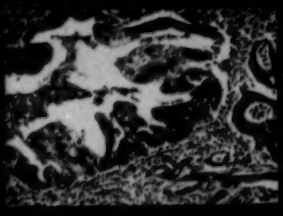
POLYPOID MALIGNANCY THAT COULD HAVE BEEN DETECTED BY ENDOSCOPY AT TIME OF RESECTION




REMOVAL AT BASE
A
B
EXCISED SPECIMEN
REMOVAL WITH MUCOSAL BASE
A
B
1st row
2nd row
A
B
A CLOSURE - VERTICAL
A CONTINUOUS SUTURE
A INTERRUPTED SUTURE
2nd row
1st row
A CLOSURE - TRANSVERSE
B EPIPLOIC APPENDAGE COVERING SUTURE LINE
A
B
PROBLEM OF SEGMENTAL RESECTION VERSUS POLYPECTOMY IS IN PROGESS OF ASSESSMENT

RESECTION FOR SESSILE ADENOMAS



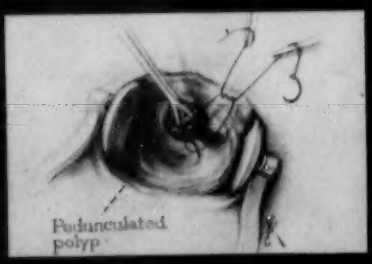


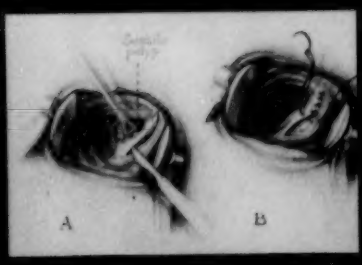
PRESURGICAL PREPARATION

CONSISTS OF CLEANSING OF THE COLON AND THE ORAL ADMINISTRATION OF A SOLUBLE ANTIBIOTIC (OXYTETRACYCLINE) OR ENTEROBIOTIC TABLETS (A COMBINATION OF OXYTETRACYCLINE AND NEOMYCIN) GIVEN FOR 2 DAYS

ALL SESSILE ADENOMAS LOCATED ABOVE THE REACH OF THE 25 cm SIGMOIDOSCOPE SHOULD BE TREATED BY APPROPRIATE INTESTINAL RESECTION (SO AS NOT TO MISS A HIDDEN CANCER)

EXCISION VIA ANAL CANAL





ADVISED, (1) FOR THOSE SURGEONS WHO ARE NOT EXPERT IN THE USE OF ELECTROSURGICAL ARMAMENTARIUM, AND
(2) WHENEVER INDURATION OF ADENOMAS IS SUSPECTED ON DIGITAL EXAMINATION

FOLLOW-UP OBSERVATION

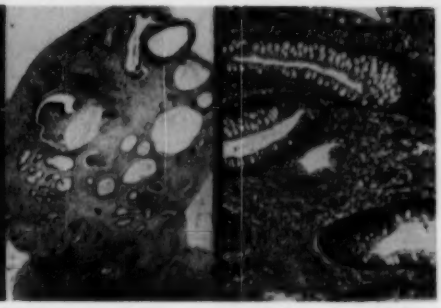
PERIODIC ENDOSCOPIC AND ROENTGENOGRAPHIC EXAMINATIONS ARE MADE FOR THE LIFETIME OF ALL PATIENTS IN WHOM ADENOMAS HAVE BEEN REMOVED WITH A VIEW TO DETECTING NEW OR RECURRENT LESIONS AT THE EARLIEST POSSIBLE TIME. THE SMOOTH ADENOMAS ARE FOLLOWED ENDOSCOPICALLY EVERY 2 MONTHS FOR THE FIRST 6 MONTHS AND ONCE IN 6 MONTHS THEREAFTER. THE VILLOUS ADENOMAS ARE FOLLOWED SIGMOIDOSCOPICALLY MONTHLY FOR FROM 3 TO 6 MONTHS, THEN ONCE EVERY 3 TO 4 MONTHS.

RADIOGRAPHY IS PERFORMED ONCE EVERY 12 TO 18 MONTHS ON ALL PATIENTS.

PEDIATRIC ASPECTS

JUVENILE ADENOMAS PRESENT A MICROSCOPIC ARCHITECTURE SIMILAR TO THAT OF ADENOMAS IN THE ADULT EXCEPT FOR A GREATER AMOUNT OF CONNECTIVE TISSUE STROMA (A) AND A GREATER AMOUNT OF INFLAMMATORY CELL INFILTRATION (B). MALIGNANCY IN ADENOMAS OF INFANTS OR CHILDREN HAS NOT BEEN OBSERVED BY US TO DATE.

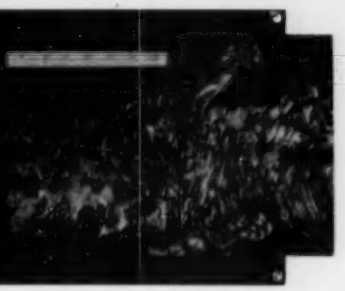
THE TREATMENT OF JUVENILE ADENOMAS IS ESSENTIALLY THE SAME AS THAT FOR BENIGN ADENOMAS IN ADULTS.

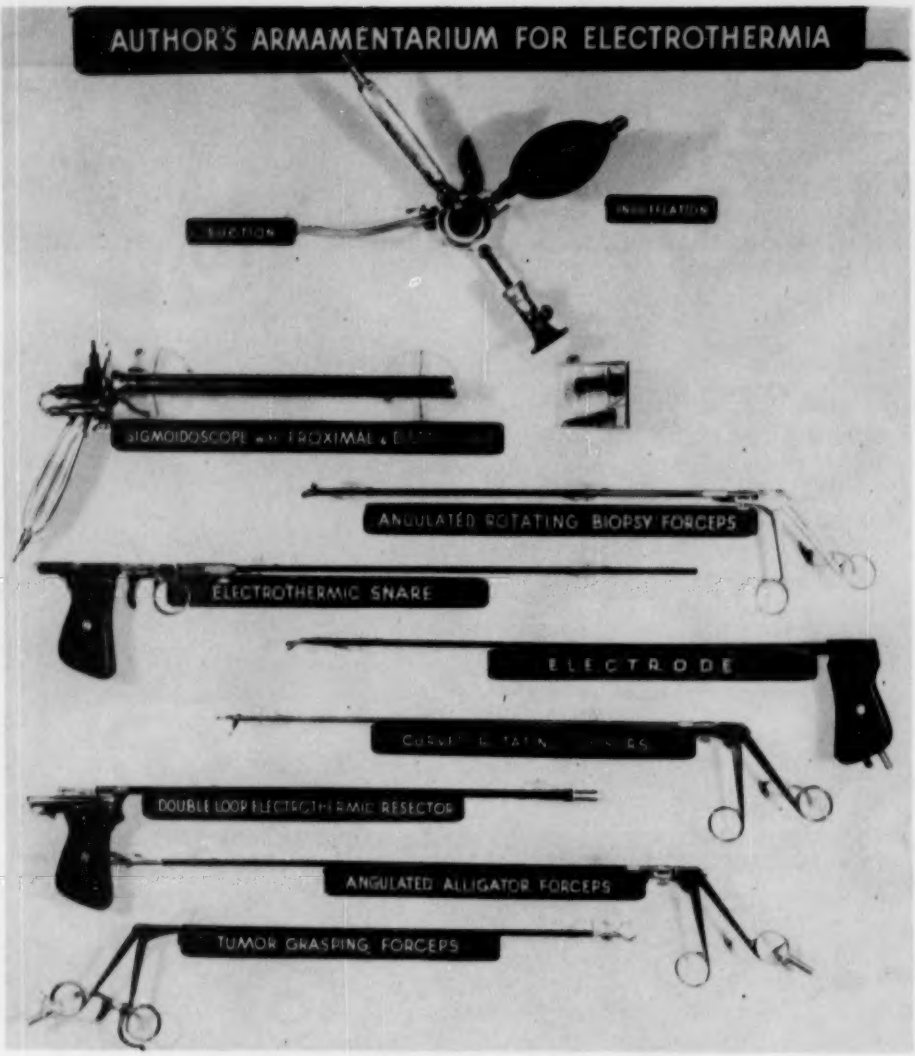


ADENOMAS IN COLITIS

A SOLITARY TRUE ADENOMA SITUATED WITHIN THE REACH OF THE SIGMOIDOSCOPE MAY BE MANAGED LIKE THE ONE ENCOUNTERED IN UNINFLAMED COLONS.

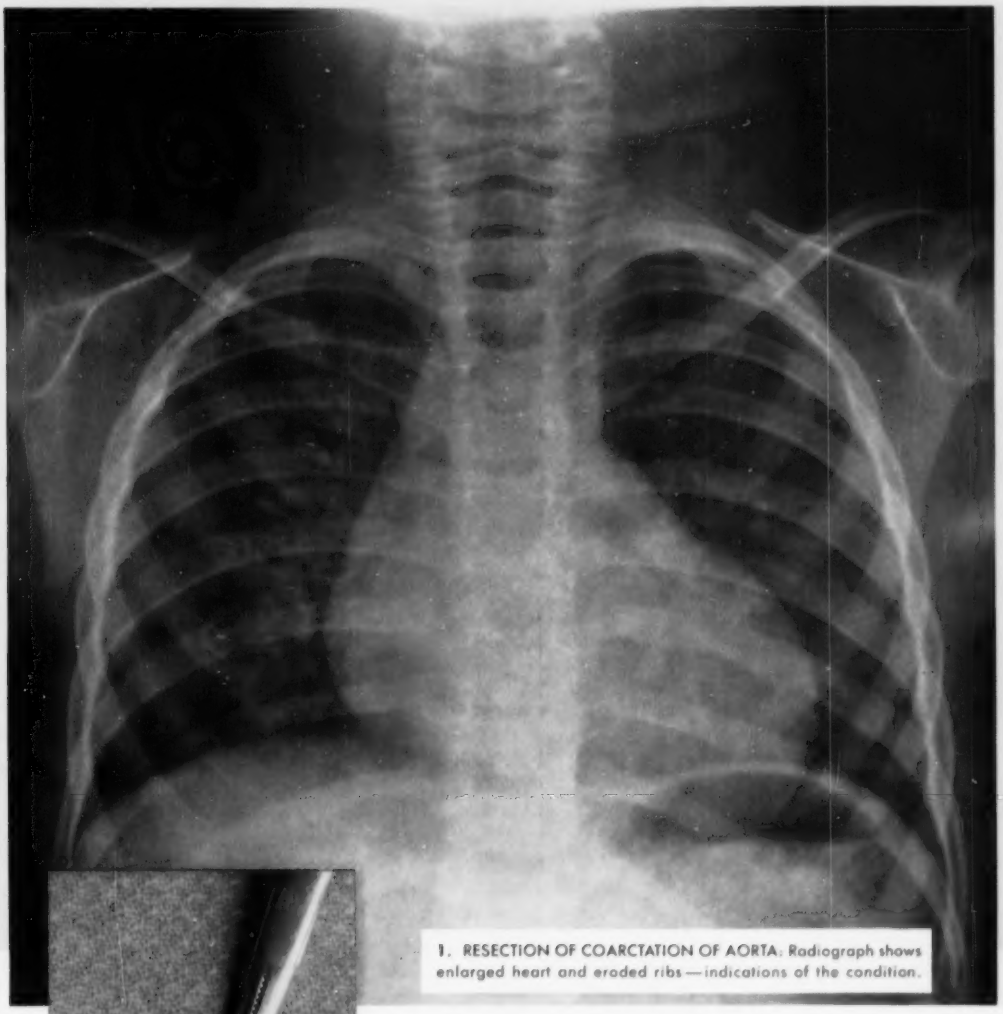
AN ADENOMA LOCATED ABOVE THE REACH OF THE SIGMOIDOSCOPE, OR WHEN MULTIPLE, IS BEST ERADICATED BY TOTAL COLECTOMY BECAUSE THE CHANGES OF THE DEVELOPMENT OF A MALIGNANCY ARE COMPOUNDED BY 2 CANCER POTENTIALS - THE COLITIC PROCESS AND THE ADENOMA'S PROPENSITY TO UNDERGO MALIGNANT DEGENERATION.



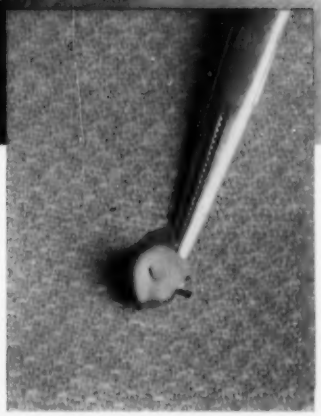

AUTHOR'S ARMAMENTARIUM FOR ELECTROTHERMIA
SUCTION
INSUFFLATION
SIGMOIDOSCOPE
ANGULATED ROTATING BIOPSY FORCEPS
ELECTROTHERMIC SNARE
ELECTRODE
DOUBLE LOOP ELECTROTHERMIC RESECTOR
ANGULATED ALLIGATOR FORCEPS
TUMOR GRASPING FORCEPS

Thanks to radiography and photography

physicians and students can review this classic case...



1. RESECTION OF COARCTATION OF AORTA. Radiograph shows enlarged heart and eroded ribs—indications of the condition.



2. Resected coarctate segment of the aorta. *Turn page for color illustrations of surgery.*

With the visual data reproduced on these pages—preoperative radiograph of the patient's condition, color photographic record of the surgical procedure—the attending physician, the radiologist and the surgeon have material for discussion, for teaching and research, for publication and exhibition. Like ripples from a pebble thrown in the water, experience becomes an ever-widening force!

Kodak
TRADE MARK

Anytime — anywhere — physicians, students, researchers who have access to the material shown here, can study this case, view the radiographs, review the steps in surgery, learn from the problem and its solution.

The cost of this visual data? Small in comparison to its great educational value!

For Radiography: Kodak Blue Brand X-ray Film and Kodak x-ray processing chemicals meet the most exacting requirements. They are always dependable—uniform. Quality-controlled—rigidly tested—they are made to work together.

For Color Photography: Kodachrome Films for miniature and motion-picture cameras; Kodak Ektachrome Films and Kodak Ektacolor Films for sheet-film cameras; Kodak Ektachrome Films for roll-film and miniature cameras; Kodacolor Films for roll-film cameras and cameras accepting No. 828 film. Kodak color print materials are also available.

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from your x-ray dealer, photographic products
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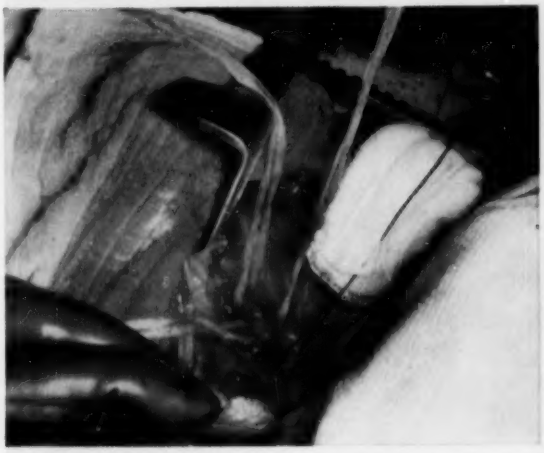
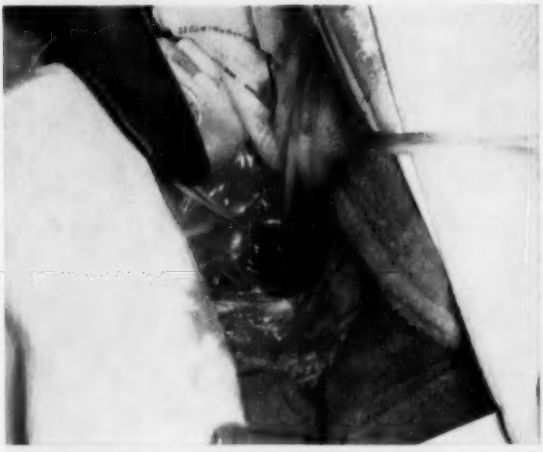
Kodak
TRADE MARK



3. Exposure of coarctation and *ligamentum arteriosum*.



4. Coarctation of aorta with distal dilatation and large intercostal arteries.

5. Completion of end-to-end anastomosis of aorta following resection of the coarctation.

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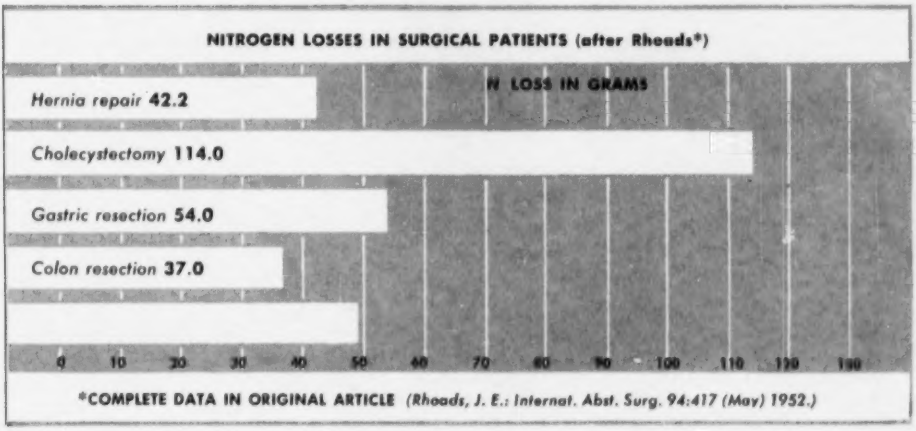
NITROGEN LOSSES IN SURGICAL PATIENTS (after Rhoads*)
N LOSS IN GRAMS
Hernia repair 42.2
Cholecystectomy 114.0
Gastric resection 54.0
Colon resection 37.0
0 10 20 30 40 50 60 70 80 90 100 110 120 130
*COMPLETE DATA IN ORIGINAL ARTICLE (Rhoads, J. E.: Internat. Abst. Surg. 94:417 (May) 1952.)

Patients about to undergo extensive surgery[1] frequently have negative nitrogen balance and protein deficiency. And after any severe trauma, including extensive surgery, the rate of protein breakdown is increased.

It is also well recognized that patients with a strongly negative nitrogen balance are much more prone to suffer delayed wound healing[2], secondary infections[3], shock[2] and delayed convalescence[4].

The need for an effective protein anabolic agent is stated by Moore and Ball[5]—"there is one unbreakable rule of surgical convalescence: to complete his recovery, regain strength and return to work the patient *must* come into positive nitrogen balance."

Nilevar (brand of norethandrolone) is a new anabolic steroid which rapidly and effectively reverses or diminishes excessive protein catabolism and nitrogen loss accompanying major surgical procedures. The protein anabolic activity of Nilevar is specific. There are usually minimal or no androgenic side effects.

In addition to its use both preoperatively and postoperatively, Nilevar is indicated in all conditions in which excessive protein catabolism (nitrogen loss) hinders or delays convalescence:

Recovery from pneumonia, poliomyelitis, severe burns and fractures, and in the care of premature infants, decubitus ulcers and wasting diseases such as cancer and tuberculosis.

The daily adult dose is three to five Nilevar tablets (30 to 50 mg.). For children the daily dosage is 1 to 1.5 mg. per kilogram of body weight for the first ten days of treatment, after which the daily dosage should be reduced in all prepuberal patients to 0.5 mg. per kilogram of body weight. Individual dosages depend on the need for and the response to therapy. G. D. Searle & Co., Chicago 80, Illinois. Research in the Service of Medicine. References supplied on request.

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